CHAPTER 1

EPOXIDE MIGRATION (PAYNE REARRANGEMENT) AND RELATED REACTIONS

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CONTENTS

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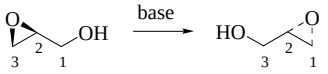
This chapter is dedicated to the memory of the late Prof. Bryant Rossiter of Brigham Young University, who was writing a chapter on the Payne rearrangement for *Organic Reactions* at the time of his death in 1995.

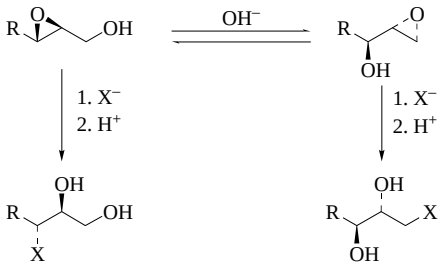
INTRODUCTION

Under a variety of basic conditions, 2,3-epoxy alcohols rearrange with inversion at C-2 (Eq. 1). The reaction, originally referred to in the literature as the *β-oxanol rearrangement*,[1] is now exclusively referred to as *epoxide migration*[2] or *Payne rearrangement.*[3,4]



(Eq. 1)

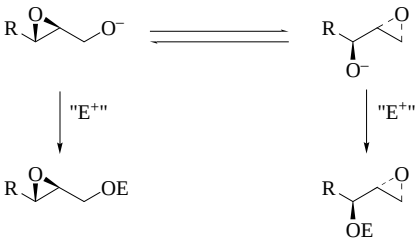
Epoxide migration is reversible, often leading to a mixture of epoxy alcohol isomers. Furthermore, in the presence of hydroxide or other nucleophiles, in situ opening of the equilibrating species may be observed (Scheme I). When such opening is desired, epoxide migration becomes a powerful method for the introduction of functionality into a substrate containing a 2,3-epoxy alcohol moiety. However, when opening is not desired, epoxide migration can become a significant problem.



Scheme I

The epoxide migration process lends itself to other synthetically useful manipulations. For example, the anionic equilibrating species may also be trapped with electrophiles such as alkyl and silyl halides, alkyl sulfonates, and epoxides

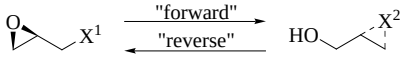
(Scheme II). Electrophilic trapping may be inter- or intramolecular, and has been used as a means of delivering functionality to either C-2 or C-3 selectively.



Scheme II

The intent of this chapter is to provide a comprehensive review of epoxide migration, including factors influencing the equilibrium position, conditions leading to in situ epoxide opening, and examples of electrophilic trapping. The reaction is discussed in relation to its utility as a synthetic method as well as its prevention as an unwanted side reaction.

Related rearrangements in which either the epoxide or hydroxy oxygen has been replaced with nitrogen or sulfur have also been studied (Eq. 2). These reactions, referred to in the literature as aza-Payne and thia-Payne rearrangements, respectively, are comprehensively included in this chapter as well. For the purposes of this discussion, the term "forward" aza-Payne rearrangement refers to the direction of reaction leading from oxirane to aziridine. Similarly, "forward" thia-Payne rearrangement refers to the direction of reaction leading from oxirane to thiirane. In the case of aza-Payne rearrangements, both forward and reverse reactions have been effected, and in this chapter the term "reverse" aza-Payne rearrangement refers to reactions leading from aziridine to oxirane.



X^1	X^2	Direction
NH_2	NH	forward
NHR	NR	forward
NHBoc	NBoc	forward
NR_2	NR_2^+	both
NHMs, NHTs	NMs, NTs	both
SAc	S	forward
SR	SR^+	forward
SPh	SPh^+	forward

(Eq. 2)

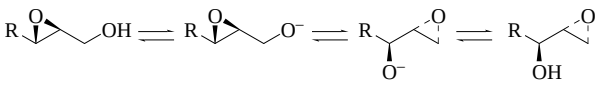
Epoxides have long been considered important in the chemistry of carbohydrates, and epoxide migration in the context of carbohydrate chemistry has been discussed

in several reviews.[5–14] In addition, particularly since discovery of the catalytic asymmetric epoxidation of allylic alcohols[15] and the rise in importance of enantiomerically enriched acyclic epoxy alcohols, epoxide migration with in situ opening in acyclic systems has been much studied. A recent chapter of *Organic Reactions* discusses epoxide migration with in situ opening in the context of asymmetric epoxidation.[16] Two reviews of the stereoselectivity and regioselectivity observed for the opening of selected acyclic epoxy alcohols derived from asymmetric epoxidation are also available.[4,17] Reviews relating specifically to aza-Payne rearrangements[18–20] and thia-Payne rearrangements[18,21] have been published. However, to date there is no comprehensive review of epoxide migration, aza-Payne rearrangements, or thia-Payne rearrangements. The tabular survey summarizes the literature of epoxide migration and related reactions, including equilibration, in situ opening and trapping, aza-Payne rearrangements, and thia-Payne rearrangements, from 1931 to 1999. Reports referring to reactions involving addition at C-1 or C-3 without inversion of stereochemistry at C-2 as "Payne rearrangements" are not covered in this review.[22,23]

MECHANISM AND STEREOCHEMISTRY

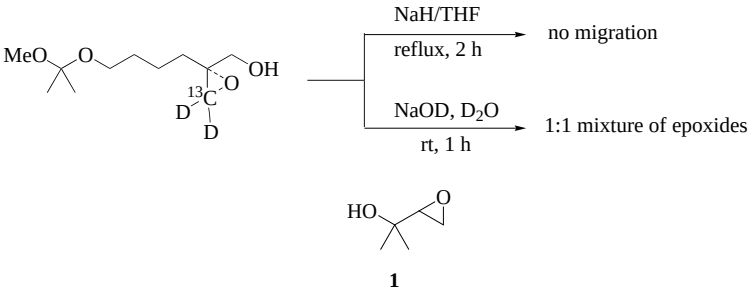
Epoxide Migration

Proposed Mechanism. The vast majority of epoxide migrations have been carried out in the presence of strong base in protic (usually aqueous) media. The accepted mechanism of epoxide migration under these conditions, first proposed by Angyal and Gilham in 1957,[2] involves deprotonation of the epoxy alcohol to form an alkoxide followed by direct intramolecular displacement at the adjacent epoxide center. An isomeric alkoxide with inverted stereochemistry is produced (Eq. 3). Reprotonation of this alkoxide by solvent completes the reaction.



(Eq. 3)

However, the mechanism of epoxide migration is almost certainly not this simple. In particular, the migration itself seems to depend strongly upon solvent, as the example in Eq. 4 indicates. In tetrahydrofuran using sodium hydride to deprotonate the alcohol, there is no evidence of reaction even after refluxing for 2 hours. In aqueous medium using sodium hydroxide as the base, the migration is complete within 1 hour at room temperature.[24] Thus, although epoxide migration requires deprotonation, deprotonation in and of itself does not necessarily lead to epoxide migration. Similarly, reaction of epoxide **1** with sodium hydride in tetrahydrofuran for 1.5 hours at 10° returned only starting material.

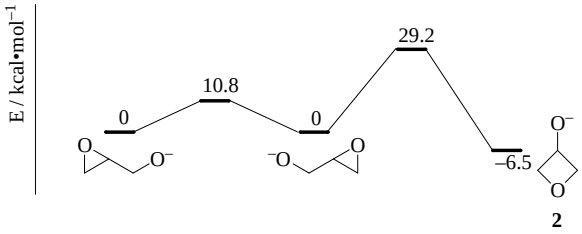


(Eq. 4)

1

It is important to realize that equilibration under protic conditions involves the protonated epoxy alcohols, while equilibration under aprotic conditions using an irreversible base such as sodium hydride does not. It has been suggested that under aprotic conditions, association of the metal cation with the initial alkoxide prevents further isomerization.[3] Nonetheless, numerous examples of epoxide migration under aprotic conditions do exist.[25,26] No mechanistic or theoretical studies have addressed the issue of solvent or counterion effect in epoxide migration.

Thermodynamic vs. Kinetic Control. Theoretical calculations at the G2 level suggest that all epoxide migrations are technically the result of kinetic rather than thermodynamic control.[27,28] Thus, as depicted in Figure I, for the anion of 2,3-epoxypropanol in the gas phase, the lowest energy isomer is not an epoxide at all. Rather, it is oxetane **2**.[28] In a mass spectrometer there is enough energy to effect an equilibration among all three of these species.[28] In solution there is far less energy available, and the oxetane isomer has never been observed in the solution-phase product mixture of epoxide migration. Thus, in solution, epoxide migration per se may be considered to be under local thermodynamic control.



2

Figure I

The selectivity of opening of equilibrating epoxy alcohols is governed by the Curtin-Hammett principle.[29] Thus, while two equilibrating epoxy alcohol isomers may be of similar energy, the product of epoxide migration and opening may not reflect this, because opening is generally a considerably slower process than migration (Figure II). Thus, epoxide migration *with opening* is under kinetic control, with selectivity governed by the slow opening of relatively rapidly equilibrating epoxy alcohol species.

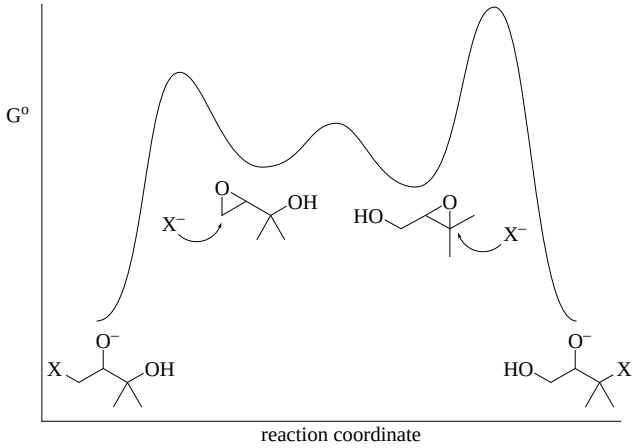
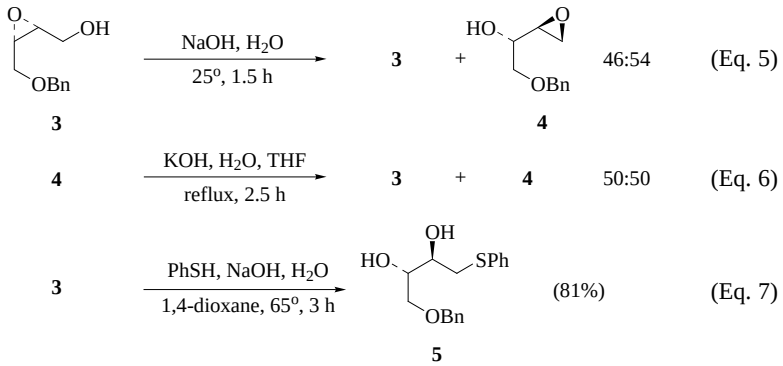


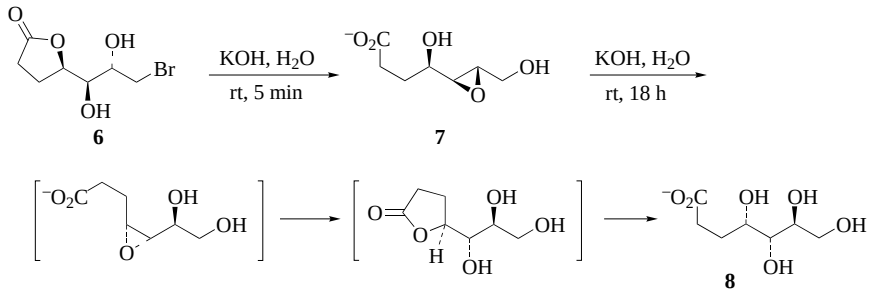
Figure II

For example, consider Eqs. 5, 6, and 7. Treatment of either epoxide **3**[25] or its rearranged isomer **4**[30] with aqueous base leads to a roughly 1:1 ratio of isomers. Thus, these two isomers are of approximately the same free energy. Nonetheless, treatment of epoxide **3** with base in the presence of thiophenol leads to an 81% yield of sulfide **5**, the product of epoxide migration to monosubstituted epoxide **4** followed by selective opening at the less substituted position.[31]



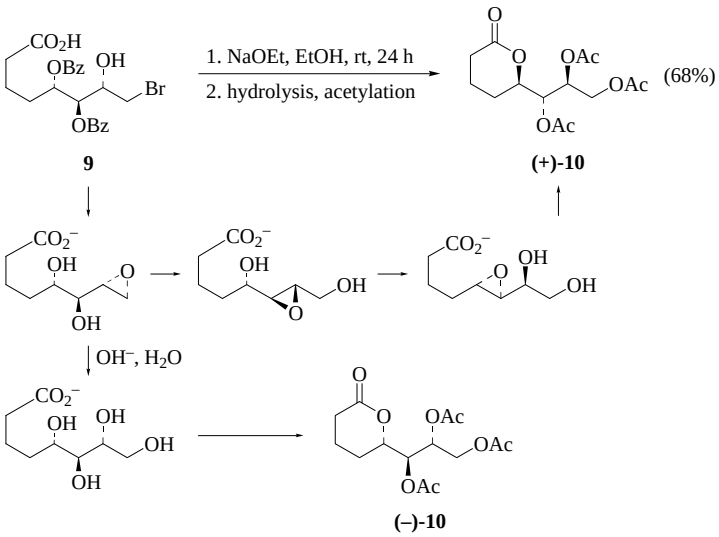
Stereochemical Considerations. Epoxide migration by definition involves stereochemical inversion at C-2. Extensive work with carbohydrates has demonstrated that multiple epoxide migrations may occur for substrates with more than one hydroxy group, leading to multiple stereochemical inversions. For example, treatment of lactone **6** (Scheme III) with aqueous potassium hydroxide for 5 minutes results in the quantitative formation of epoxide **7**, the product of bromide displacement and one epoxide migration.[32] However, with prolonged exposure to hydroxide, this product is completely converted into tetraol **8**, the product of a second epoxide

migration (to give a *cis*-disubstituted epoxide), intramolecular opening of the epoxide by the carboxylate to form a lactone, and hydrolysis. Note that all three stereocenters in the substrate have been inverted.



Scheme III

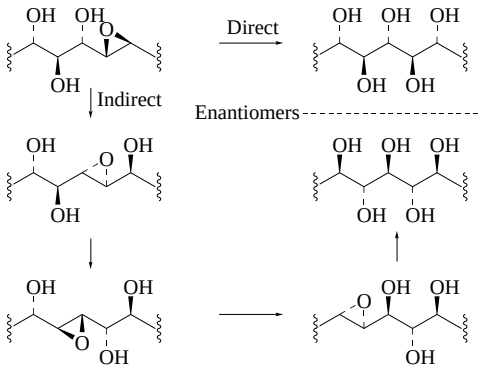
A closely related study involved the conversion of carboxylic acid **9** into lactone **10** (Scheme IV).[33] In this and related cases[34] it was found that the solvent has to be scrupulously anhydrous for effective epoxide migration. If it is not, then direct reaction of the initially formed terminal epoxide with hydroxide ion competes with epoxide migration. In that case, no stereocenters are inverted, and the competitive pathway leads to a decrease in enantiomeric excess.



Scheme IV

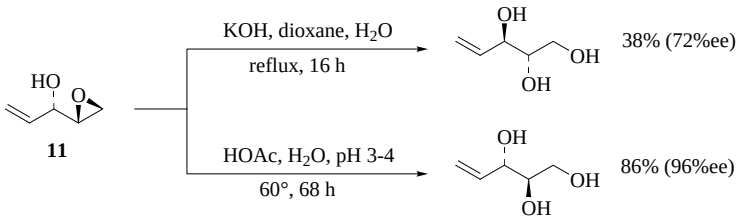
In fact, whenever epoxide migrations are effected in the presence of hydroxide, an additional stereochemical concern must be addressed. Specifically, when the

stereocenters in the substrate consist solely of the carbons involved in epoxide migration, then, as illustrated in Scheme V, opening with and without epoxide migration may lead to full or partial racemization.[35] (Scheme V is a generalization of the case in Scheme I when X=OH.)



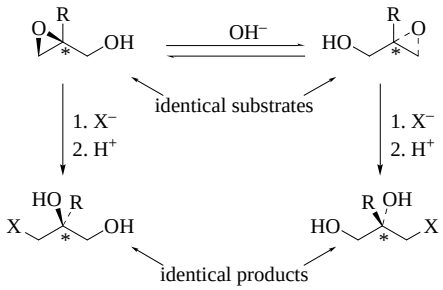
Scheme V

As a further example, consider epoxy alcohol **11** (Scheme VI). Treatment with potassium hydroxide in aqueous dioxane produces a roughly 6:1 mixture of enantiomers.[36,37] The major isomer in this case is the result of epoxide migration, while the minor isomer is the result of direct addition of hydroxide at the terminal carbon. However, mild acid treatment results in direct opening at the terminal position without migration, preserving the high enantiomeric purity of the substrate.



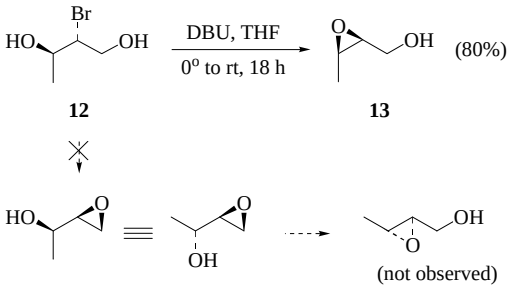
Scheme VI

In the special case of pseudo-symmetrical epoxy alcohols with only one stereocenter (necessarily at C-2), nucleophilic opening both with and without epoxide migration gives the same product (Scheme VII). This special degeneracy has been exploited in syntheses involving glycidol (R=H).[38,39]



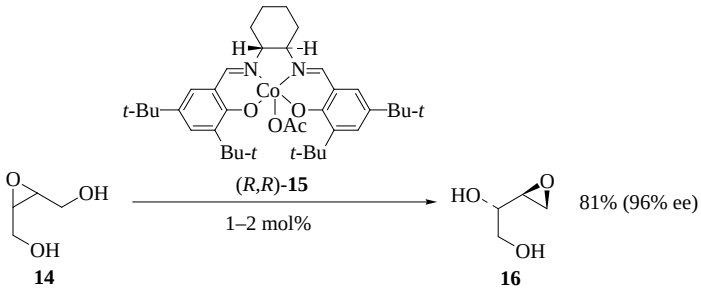
Scheme VII

The regioselectivity of in situ epoxide formation can also play an important role in dictating the stereochemical outcome of epoxide migration.[14,40] For example, treatment of bromodiol **12** with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) gives the cis-disubstituted epoxy alcohol **13** exclusively (Scheme VIII).[41] Had the primary alcohol displaced the bromide, the outcome would have been completely different. Note that DBU is not effecting epoxide migration itself. Indeed, the observed product is only slightly favored at equilibrium relative to its rearranged counterpart.[3,42] Such kinetic selectivity for disubstituted over primary epoxide formation prior to epoxide migration is well documented in the carbohydrate literature.[43–45]



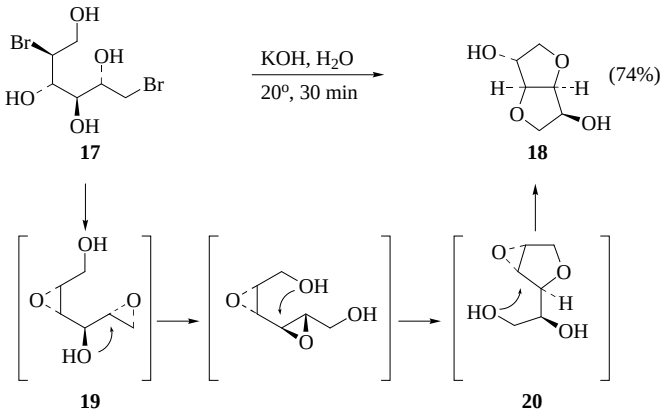
Scheme VIII

Epoxide Migration Under Nonbasic Conditions. Despite the fact that complex mechanisms involving "epoxide migration" under acidic conditions have occasionally been proposed,[46–52] work with carbohydrates has demonstrated conclusively that epoxide migration under acidic conditions is not generally observed.[53,54] However, a recent report of epoxide migration under nonbasic conditions involves treatment of *meso* diol **14** with 1–2 mol% of the chiral cobalt(III) complex (*R,R*)-**15** (Eq. 8) to give 1,2-diol **16** in high yield and enantiomeric purity.[55] This result suggests that catalytic kinetic resolution of epoxy alcohols might be effected with chiral epoxide migration catalysts.



(Eq. 8)

Nucleophilic Trapping in situ. Many examples of in situ nucleophilic trapping of epoxide migration products have been reported, and many of these are intramolecular, such as illustrated in Schemes III and IV. A related example (Eq. 9) involves treatment of dibromide **17** with aqueous potassium hydroxide.[45] Within 30 minutes at 20°, **17** is converted to bicyclic ether **18** in over 70% yield, presumably via intermediates **19** and **20**. Note that both epoxide openings are favored *exo*-openings.[56] Since all four stereocenters in the substrate take part in the epoxide migration, all end up inverted.



(Eq. 9)

Electrophilic Trapping in situ. Electrophilic trapping of epoxy alcohols after epoxide migration involves selective reaction of the hydroxy group of one of the equilibrating isomers (Scheme II). Specific reactions are discussed below, in the context of the scope of epoxide migration.

Aza-Payne Rearrangements

The proposed mechanisms for aza-Payne rearrangements are considerably more varied than those for epoxide migration because of two factors. First, with the added nitrogen atom, there are two distinct directions of reaction—"forward" (toward aziridine) and "reverse" (toward oxirane). Second, variation of the aziridine nitrogen substituent significantly affects the mechanism of the reaction.

Forward and reverse reactions carried out under basic conditions are presumed to follow a pathway analogous to Eq. 3. Forward reactions employing Lewis acids are presumed to be initiated by activation of the oxygen of the oxirane by the Lewis acid followed by aziridine formation.

Theoretical gas-phase calculations (MP2/6−31+G* single-point energies at RHF/3−21+G* optimized geometries, Figure III)[57] suggest that for the parent substrate, the aziridine isomer **21** lies approximately 5 kcal/mol in energy above the oxirane **22**. Deprotonation, however, would be expected to favor the aziridine by virtue of the lower energy of oxy anion **23** relative to aza anion **24**.

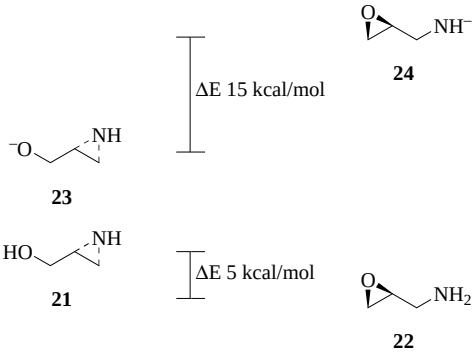
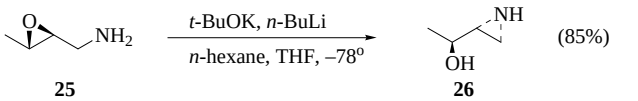


Figure III

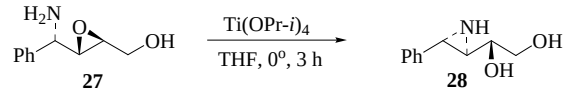
Experimentally it is observed that deprotonation of epoxy amines results in rearrangement to the aziridine. For example, deprotonation of oxirane **25** with *n*-butyllithium/potassium *tert*-butoxide[58] (Eq. 10) gives aziridine **26** in 85% yield after quenching.[57] A number of other bases, including sodium hydride, potassium hydride, and potassium *tert*-butoxide, were ineffective.



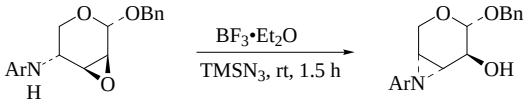
(85%) (Eq. 10)

The equilibrium between epoxy amine and aziridine alcohol can also be driven toward aziridine by complexation with titanium(IV),[59] boron trifluoride,[60] trimethylaluminum,[61] or trimethylsilyl triflate.[62] Examples include oxirane **27** rearranging to aziridine **28** upon treatment with titanium(IV) isopropoxide (Eq. 11),[59] 4-(*tert*-butoxycarbonyl)phenyl-protected ribopyranoside **29** rearranging to aziridine **30** upon treatment with boron trifluoride etherate in trimethylsilyl azide (Eq. 12),[60] and epoxy amine **31** rearranging to aziridine alcohol **32** upon treatment with butyllithium/trimethylaluminum (Eq. 13).[61] No evidence exists that these rearrangements

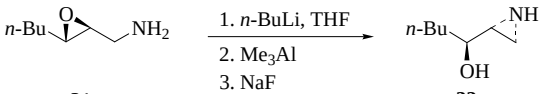
under Lewis acid conditions are reversible equilibria. Rather, it appears that complexation with oxygen drives the reaction to the aziridine isomer. No detailed mechanistic or theoretical work has been done in this area.



27 **28** (63%) (Eq. 11)

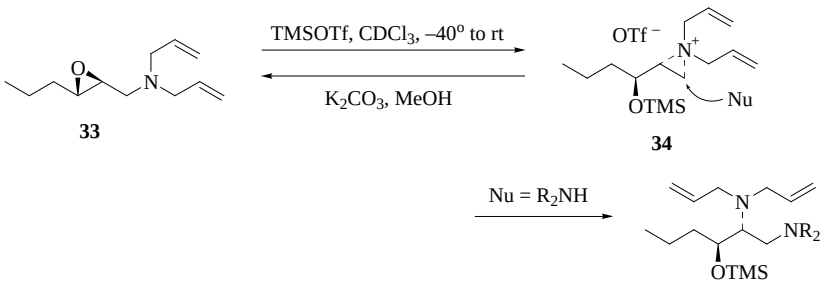


29 **30** (60%) (Eq. 12)



31 **32** (72%) (Eq. 13)

When trimethylsilyl triflate is employed in forward aza-Payne rearrangements of epoxy amines, in situ opening may be effected (Scheme IX). The formation of an aziridinium ion has been observed for the reaction of epoxy amine **33** using ^{1}H NMR spectroscopy.[62] Treatment of aziridinium ion **34** with methanolic K_2CO_3 regenerates epoxide **33**; treatment with a broad variety of amine nucleophiles leads to opening.



33 **34**

Scheme IX

If the nitrogen is activated as a sulfonamide, then calculations suggest that the energy picture is considerably different (Figure IV).[57] Once again the more stable neutral species is the epoxide, **35**, rather than the aziridine, **36**. However, now the more stable anion (at least in the gas phase) is predicted to be aza anion **37** rather than oxy anion **38**.

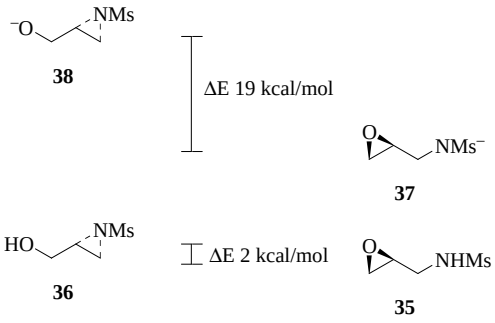
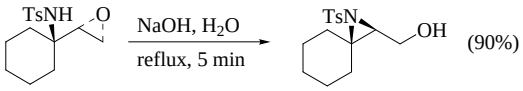


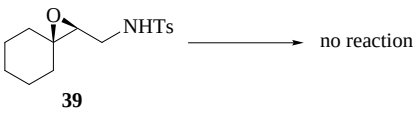
Figure IV

In practice, results for sulfonamides depend strongly upon substrate structure and conditions. In aqueous solution, where deprotonation is reversible, the structure of the substrate critically determines the equilibrium ratio.[57,63] However, consistent with these calculations, use of irreversible hydride bases such as sodium hydride or potassium hydride in polar aprotic solvents (dichloromethane or tetrahydrofuran/hexamethylphosphoric triamide mixtures) leads to a preponderance of the oxirane.[57,64]

In selected cases, however, brief treatment with refluxing aqueous sodium hydroxide converts epoxy sulfonamides into the aziridines (Eq. 14).[63] Structural factors are clearly at work here. No rearrangement was seen for primary sulfonamide **39** (Eq. 15); prolonged treatment led to decomposition.



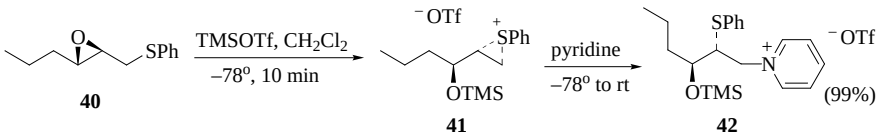
(Eq. 14)



(Eq. 15)

Thia-Payne Rearrangements

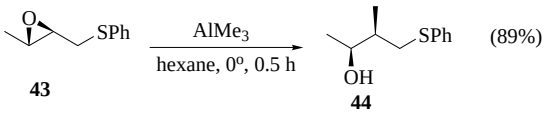
All reported thia-Payne rearrangements have been in the "forward" direction, starting with a 2,3-epoxy sulfide. Except for a single report,[65] these rearrangements have been carried out under Lewis-acidic conditions that have led to opening. Treatment, for example, of epoxide **40** with trimethylsilyl triflate (Eq. 16) produces an intermediate thiiranium salt (**41**), which is then opened with pyridine to form the pyridinium salt **42** in quantitative yield.[66]



40 **41** **42**

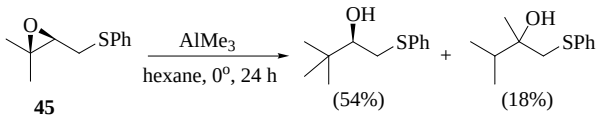
(Eq. 16)

When aluminum reagents are used, both reduction and carbon-carbon bond forming reactions are made possible.[67,68] However, the regiochemistry of opening with aluminum reagents is unlike that found in epoxide migrations and aza-Payne rearrangements, and it is sensitive to both substrate and reagent. For example, with trimethylaluminum, opening of epoxide **43** occurs at C-2 with retention (actually double inversion) exclusively to give alcohol **44** (Eq. 17).[67] Substrates prone to carbocation formation at C-3, such as epoxide **45**, undergo reactions that probably do not involve thiiranium intermediates (Eq. 18).



43 **44**

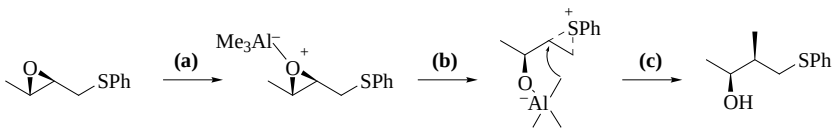
(Eq. 17)



45

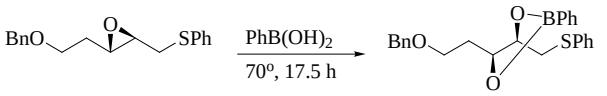
(Eq. 18)

The proposed mechanism for the reaction of epoxy sulfides with trimethylaluminum (Scheme X) involves (a) complexation of the aluminum reagent with the epoxide oxygen, (b) formation of a thiiranium ion, and (c) opening by either the internally complexed aluminum species or a second equivalent of reagent. This reactivity appears to be unique to trimethylaluminum. The more active aluminum reagents, 1-hexenyl(diisobutyl)aluminum, diethyl(1-hexynyl)aluminum, and diisobutylaluminum hydride (DIBAL), all tend to open the thiiranium ion at the less substituted terminal position.



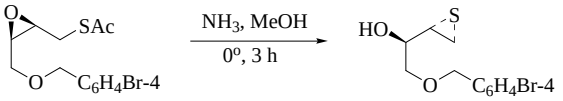
Scheme X

Excellent selectivities at C-2 have also been observed for opening of 2,3-epoxy sulfides with phenylborinic acid (Eq. 19).[69] Again, double inversion is observed.



(Eq. 19)

The single report of a thia-Payne rearrangement not involving a Lewis acid is the reaction of thioacetate **46** with ammonia to produce thiirane **47** in 89% yield (Eq. 20).[65]



46 **47**

(Eq. 20)

SCOPE AND LIMITATIONS

In general, epoxide migration requires strongly basic conditions such as sodium hydroxide/water[3] or sodium methoxide/methanol.[54] Despite reports of their general inappropriateness,[3,24] aprotic conditions such as butyllithium/lithium chloride/tetrahydrofuran,[25] sodium hydride/tetrahydrofuran with[25] and without[26] [18]-crown-6, and lithium chloride/tetrahydrofuran[25] have been utilized with limited success. This narrow range of conditions places considerable limitations on the reaction.

The primary considerations in epoxide migration involve (a) direction of epoxide equilibration, (b) selectivity in epoxide opening by nucleophiles, and (c) selectivity in epoxy alcohol trapping by electrophiles. These subjects are discussed for epoxide migration, aza-Payne rearrangements, and thia-Payne rearrangements in this section. As will be seen, much research has focused on understanding the scope and limitations of epoxide migration in both cyclic and acyclic systems, and many generalizations have been made. In addition, many studies have shown that despite unfavorable thermodynamic preference for a desired epoxide, selectivity in opening can be achieved kinetically.

Direction of Epoxide Equilibration in Acyclic Systems

To a certain extent, the more stable of two isomeric acyclic epoxy alcohols is predictable based on the substitution pattern around the epoxide. Representative acyclic systems for which equilibrium has been approached from both sides under identical conditions (aqueous sodium hydroxide at room temperature) are shown in Figure V. The ratios, initially determined by gas chromatography,[3,42] have been confirmed by NMR spectroscopy.[42,70]

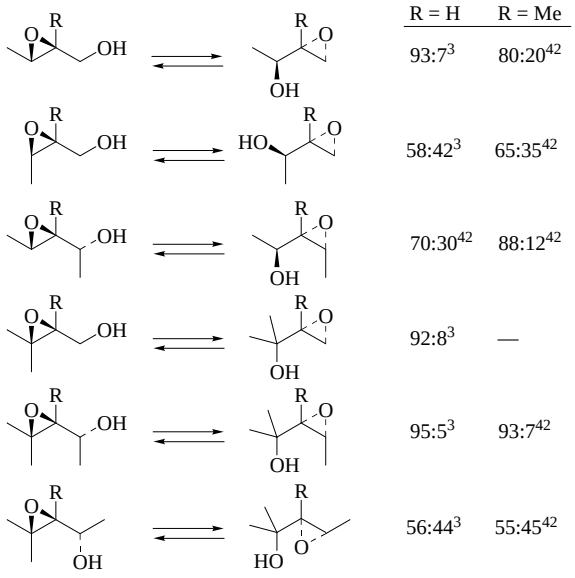
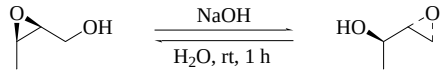
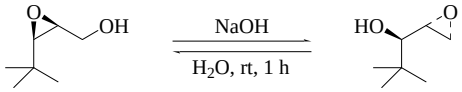


Figure V

There is significant variability in the thermodynamic product ratios due to both steric and electronic effects. For example, whereas cis-disubstituted epoxide **48** and monosubstituted epoxide **49** establish only a 58 : 42 equilibrium ratio when treated with aqueous sodium hydroxide (Eq. 21), cis-disubstituted epoxide **50** and monosubstituted epoxide **51** establish a 5 : 95 equilibrium ratio (Eq. 22).[42]

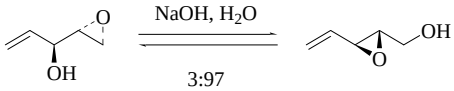


48 58:42 **49** (Eq. 21)

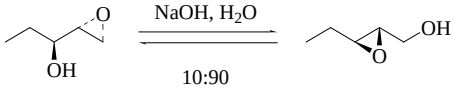


50 5:95 **51** (Eq. 22)

There is also evidence that vinyl and phenyl groups attached to the oxirane in one isomer lower its free energy relative to the other isomer, at least in comparison with simple alkyl substitution. Thus, vinyl epoxy alcohol **52** can be equilibrated to a 3 : 97 mixture with its 2,3-epoxy isomer by very careful isomerization with base (Eq. 23).[37] In comparison, isomerization of the saturated epoxy alcohol **53** gives a slightly lower selectivity (Eq. 24).[71]

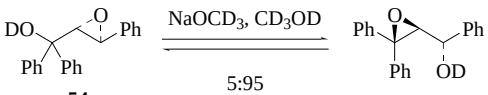


52 (Eq. 23)

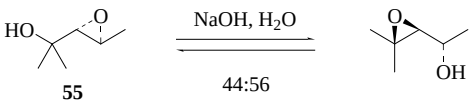


53 (Eq. 24)

A strong effect of phenyl substitution is seen in comparing the equilibrations of epoxy alcohols **54**[70] and **55**[3] (Eqs. 25 and 26).

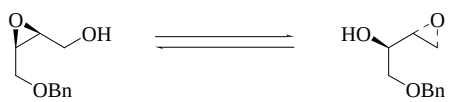


54 (Eq. 25)



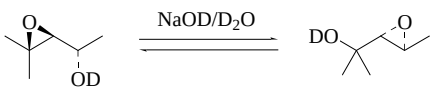
55 (Eq. 26)

Generally only subtle effects of conditions on equilibrium ratios are observed.[70] However, the equilibrium ratio between epoxy alcohol isomers **56** and **57** (Eq. 27) using typical aqueous conditions is reversed using aprotic conditions.[25] The equilibrium is driven in the direction of the cis-disubstituted oxirane isomer **56** in this case. The equilibrium ratio for the isomerization of epoxy alcohol **58** to **59** (Eq. 28) is somewhat dependent upon base concentration.[70]



56 **57** (Eq. 27)

Conditions	**56** :**57**
NaOH, H_2O, 25°, 1.5 h	46:54
NaH, 18-crown-6, THF, 25°, 12 h	75:25



58 **59** (Eq. 28)

[NaOH]	**58**:**59**
0.01 M	50:50
0.1 M	52:48
1 M	62:38

The following general observations relating to equilibrating acyclic epoxy alcohols have been reported:

(1) An isomer with higher substitution around the oxirane is favored.[3,42,70]

(2) A trans substituent on the epoxide is a stabilizing influence; a cis substituent is destabilizing.[3,42,70]

(3) An isomer with a primary hydroxy group is favored.[42]

(4) A substituent at C-2 has only secondary influence on the equilibrium.[42]

(5) Resonance-donating substituents (such as phenyl[70] and allyl[37,72]) on the oxirane are stabilizing influences (relative to the other epoxide migration isomer, not to reactivity), while electron-withdrawing substituents (such as trifluoromethyl[73]) on the oxirane are destabilizing.

(6) The concentration of base has little effect on equilibrium ratio.[70]

Direction of Epoxide Equilibration in Cyclic Systems

All reported equilibrium ratios for pyranoside epoxy alcohols where equilibrium was reached starting from both isomers under identical conditions are shown in Figure VI, although conditions vary among the five examples. Yields of isolated of pure regioisomers have been as high as 85%.[74] Note that any anomeric effect that might place the methoxy substituents in an axial orientation appears to be overshadowed substantially by the preference for equatorial hydroxyl. (That is, the methoxy group in each example is presumed to be equatorial as well, at least for predictive purposes). The situation is somewhat more complicated when the pyranoside is α-substituted (C-1 and C-5 substituents trans disposed), because in those cases simple conformational analysis appears to be of little help, and more subtle factors are involved.[75,76]

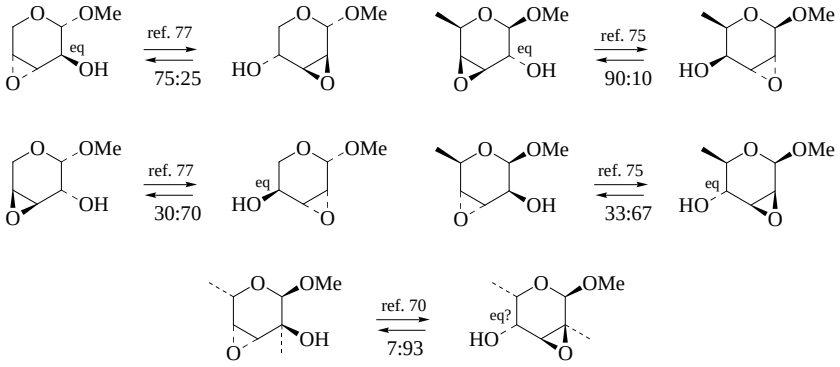


Figure VI

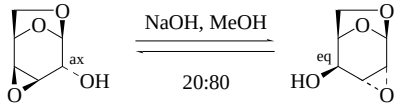
Three generalizations for pyranoside-based epoxide migrations have been made:

(1) The favored epoxide is the one with more pseudoequatorial groups, with the anomeric center substituent generally assumed to be equatorial, provided that is possible.[78]

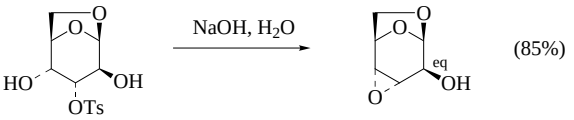
(2) Substitution trends are similar in cyclic and acyclic systems, favoring trisubstituted oxirane isomers over disubstituted ones.[70,79]

(3) There is no evidence of significant through-space interactions such as hydrogen bonding or lone-pair–lone-pair repulsions influencing the equilibrium ratio.[78]

Preference for the isomer with more equatorial groups is seen especially clearly for conformationally locked 1,6:3,4-dianhydro-β-D-*galacto*-hexopyranose **60**. Treatment of this compound with sodium hydroxide in methanol (Eq. 29) produces a 1:4 ratio of the starting material to its gulo isomer **61**.[80] Similarly, treatment of tosylate **62** with sodium hydroxide in water (Eq. 30) results in an 85% yield of isomer **63**.[81] In both cases, the favored isomer is the one with the pseudoequatorial hydroxy group.

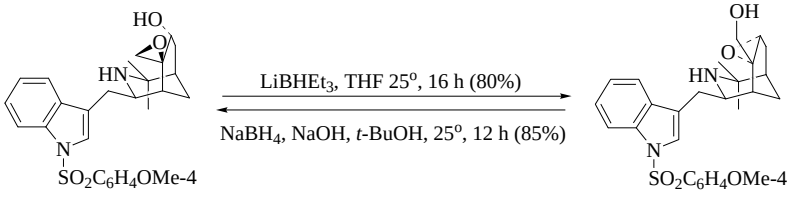


60 **61** (Eq. 29)



62 **63** (Eq. 30)

A dramatic reagent effect on epoxide migration in cyclic systems has been observed in one alkaloid synthesis (Eq. 31).[82] Attempts to reduce epoxy alcohol **64** with $LiBHEt_3$ instead resulted in epoxide migration to form isomer **65** in 80% yield, while attempts to reduce epoxy alcohol **65** with sodium borohydride instead resulted in epoxide migration to regenerate isomer **64** in 85% yield. No explanation of this unique result is provided, but it is probable that sodium borohydride in alcohol is effectively equilibrating the alcohols, while $LiBHEt_3$ under aprotic conditions involves irreversible deprotonation and equilibration favoring the primary alkoxide. This preference would be consistent with that observed for the equilibration of epoxide **56** using sodium hydride, as illustrated in Eq. 27.



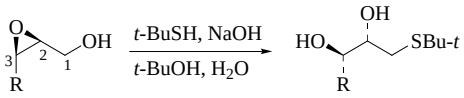
64 **65** (Eq. 31)

Selectivity of Epoxide Opening

Despite the fact that generally the more substituted epoxide is more stable, nucleophilic opening of a pair of equilibrating epoxy alcohols often can be engineered to occur primarily, if not exclusively, at the less substituted carbon of the less substituted epoxide, in accordance with the Curtin-Hammett principle (Figure II, above). Evidence suggests that in comparing monosubstituted, cis-disubstituted, and

trans-disubstituted epoxy alcohols, although the order of stability is trans > cis > mono,[3,42] the order with respect to the kinetics of epoxide opening is mono >> cis > trans.[31,83]

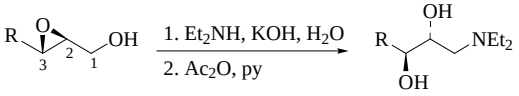
Nucleophiles investigated include hydride,[4,84] cyanide,[4,85,86] acetylide,[87–89] alkyl and alkenyl cuprates,[25,90] amines,[91,92] sulfonamides,[4] azide,[93–95] halides,[96,97] phenythiolate,[31,38,98–102] *tert*-butylthiolate,[91,103] and numerous oxygen-based nucleophiles (for references, see Table III-D). Although yields have been moderate to excellent, regioselectivity has been mixed. Notable problems involve hydride[4,84,104] and acetylide[87–89] addition, for which the principal difficulty is competitive opening at C-2; amine addition, which is complicated by competitive opening at C-1, C-2, and C-3;[91] and phenylthiolate addition, which often exhibits low selectivity relative to opening at C-1 and C-3.[38] Generally, *tert*-butylthiolate is more selective than phenylthiolate.[91] The relative amount of opening of one isomer is reduced if that isomer has additional electron-withdrawing substituents vicinal to the oxirane. For example, opening of epoxide **66** (Eq. 32) with *tert*-butylthiolate is considerably more selective than opening of epoxide **67**.



	R	% C-1 opening
66	CH_2OH	95
67	n-C_7H_{15}	66

(Eq. 32)

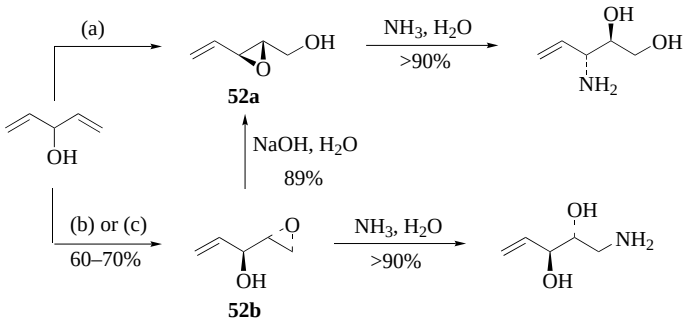
Where the alcohol or epoxide is allylic[36,37,105] or benzylic,[91] opening with and without epoxide migration often compete, even when hydroxide is the nucleophile. For example, the percent of opening of epoxide **68** (Eq. 33) at C-1 with diethylamine is considerably less than that for alkyl-substituted epoxide **69**.[91]



	R	% C-1 opening
68	Ph	12
69	n-C_7H_{15}	80

(Eq. 33)

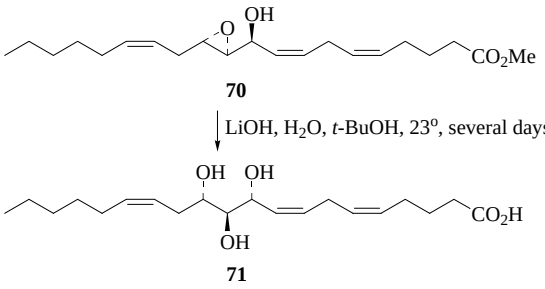
As noted above (Scheme VI), when the nucleophile is hydroxide, competitive opening at C-1 vs. C-3 can lead to a decrease in enantiomeric excess. For example, asymmetric epoxidation of divinylcarbinol (Scheme XI) gives only the product of epoxide migration (**52a**) when the original stoichiometric conditions reported for that reaction are used, including workup with sodium hydroxide.[106] When a nonbasic workup is used instead,[106] or the reaction is carried out using molecular sieves and a catalytic amount of titanium isopropoxide,[106,107] then the unrearranged product **52b** can be isolated in moderate yield. Rearrangement of **52b** to **52a** is effected by brief treatment with 0.5 M aqueous sodium hydroxide at room temperature.[37] No epoxide migration is observed when either epoxy alcohol isomer is opened with ammonia.[108,109] The high regioselectivity of these vinylic epoxide openings stands in contrast to the reaction of *trans*-2,3-epoxyhexan-1-ol with amines, which leads to a complex mixture of isomers.[91]



a: 1. Ti(OPr-*i*)$_4$ (1 eq), *t*-BuO$_2$H, L-(+)-DET, CH_2Cl_2, –20°, 3 d; 2. tartaric acid, NaOH, H_2O
b: 1. Ti(OPr-*i*)$_4$ (1 eq), *t*-BuO$_2$H, L-(+)-DET, CH_2Cl_2, –20°, 3 d; 2. H_2O/acetone, distillation
c: 1. Ti(OPr-*i*)$_4$ (0.1 eq), *t*-BuO$_2$H, L-(+)-DET, MS 4Å, CH_2Cl_2, –25°, 7 d; 2. distillation

Scheme XI

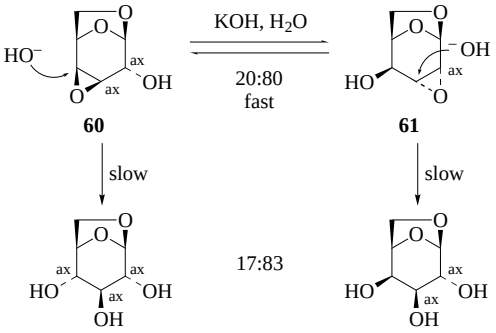
In the conversion of hepoxilin (10*S*)-HxB$_3$ (**70**) into trioxilin (10*R*,11*S*,12*S*)-TrXB$_3$ (**71**), epoxide migration precedes opening at the allylic position when lithium hydroxide is used as the base (Eq. 34).



(Eq. 34)

Where there is no allylic or benzylic activation of the epoxide, nucleophilic addition of hydroxide has been observed to occur with very high selectivity at the least substituted epoxide position.[31] Nonetheless, the reader is cautioned that reports of selective addition *of hydroxide ion* to racemic substrates can only be tentatively extrapolated to nonracemic cases,[110] since competitive addition in the racemic case has no observable effect, while competitive addition in the nonracemic case leads to a decrease in enantiomeric excess (Scheme V).

In cyclic systems such as pyranosides, the regioselectivity of epoxide opening is highly biased toward axial addition to form a (possibly transient) diaxial species. Thus, for example, both 1,6:3,4-dianhydro-β-D-*galacto*-hexopyranose (**60**) and 1,6:2,3-dianhydro-β-D-*gulo*-hexopyranose (**61**) give the same 17:83 ratio of products, both of which result from a trans-diaxial opening of the epoxide (Eq. 35).[111] Since opening is slower than equilibration, it is simply fortuitous that the product ratio is similar to the equilibrium substrate ratio of 20:80.[80]

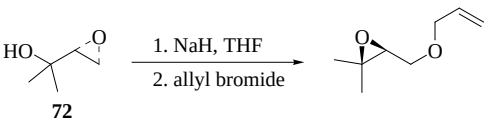


(Eq. 35)

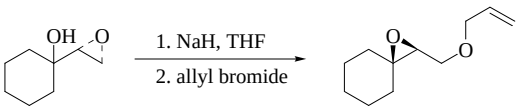
Epoxide Migration with Electrophilic Trapping in situ

One might think that it would be possible to selectively remove one isomer of an epoxy alcohol equilibrium by kinetic trapping of the less substituted alcohol with electrophiles such as alkyl halides (Scheme II). However, the few results to date that bear on this question suggest otherwise. Part of the problem may be that the anhydrous aprotic conditions generally employed in alkylations and silylations are specifically the conditions that were found in Payne's original work[3] to *not* be conducive to epoxide migration.

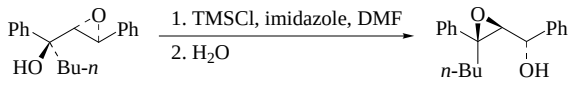
The problem is almost certainly that alkylation and silylation are generally faster processes than epoxide migration, leading to no significant equilibration. Nonetheless, two reports do suggest that in certain highly biased cases such trapping is possible (Eqs. 36–38). Specifically, deprotonation of either tertiary alcohol **72** or **73** with sodium hydride in tetrahydrofuran leads to epoxide migration and alkylation of the primary alcohol, albeit in unspecified yield.[112] Silylation of **74** with trimethylsilyl chloride and imidazole followed by hydrolysis effects its isomerization to the more highly substituted epoxide in 80% yield.[113]



72 (Eq. 36)



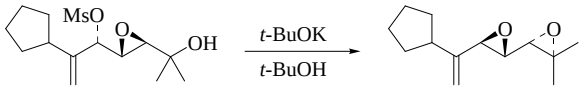
73 (Eq. 37)



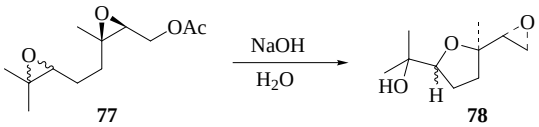
74 (Eq. 38)

Much more generally successful has been the *intramolecular* electrophilic trapping of epoxide migration isomers. Examples include the reaction of epoxide **75**

with potassium *tert*-butoxide to give diepoxide **76** (Eq. 39),[114] and the treatment of diepoxide acetate mixture **77** with aqueous sodium hydroxide to produce tetrahydrofuran **78** (Eq. 40).[115]



75 **76** (83%) (Eq. 39)



77 **78** (66%) (Eq. 40)

Rearrangement and Opening in Aza-Payne Systems

Conditions used for effecting equilibration in aza-Payne reactions are summarized in Eqs. 41 and 42.

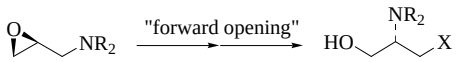
(Eq. 41)

X^1	Reagents Effecting Rearrangement Only	X^2	refs
NH_2	*n*-BuLi/*t*-BuOK	NH	57, 59, 61
NHR	*n*-BuLi/$AlMe_3$,Ti(OPr-*i*)$_4$	NR	116
NHR_2	RNH_2	NR_2^+	62
NHAr	TMSOTf	NAr	60
NHMs NHTs	BF_3•Et_2O, NaOH	NMs, NTs	63

(Eq. 42)

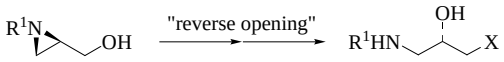
X^1	Reagents Effecting Rearrangement Only	X^2	refs
NR_2^+	NaH, K_2CO_3	NR_2	62, 117
NMs	NaH	NHMs	57
NTs	KH, NaH, NaOH, *t*-BuOLi, pyridine	NHTs	20, 57, 64, 118

Considerable experimentation has gone into discovering the best conditions for the aza-Payne rearrangement when in situ opening is desired. Again we consider both the "forward" (Eq. 43) and the "reverse" (Eq. 44) sense of reaction. Here we see the exclusive use of Lewis-acidic conditions for forward rearrangement and opening, and the use of strongly basic conditions for reverse rearrangement and opening. Of these methods, by far the most explored involve treatment of 2,3-epoxy dialkylamines with trimethylsilyl triflate[19,62,121] and treatment of *N*-tosyl-2-aziridinemethanols with potassium hydride.[20, 57, 124]



(Eq. 43)

Rearrangement/Opening Reagents	X	refs
SiO_2 / H_2O	OH	119
BF_3•Et_2O / $NaBH_3CN$	H	119
TMSOTf / amine	NH_2, NR_2	19, 62, 120, 121



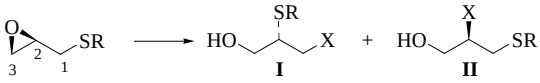
(Eq. 44)

R^1	Rearrangement/Opening Reagents	X	refs
H	KOH / H_2O	OH	122
Ts	MeCu(CN)Li•LiBr	Me	57, 64
Ts	BuCu(CN)Li•2LiCl	Bu	57
Ts	KH / $Me_2Cu(CN)Li_2$•2LiBr	Me	123, 124
Ts	KH / $Bu_2Cu(CN)Li_2$	Bu	123, 124
Ts	KH / Me_3SiCN, cat. $Yb(CN)_3$	CN	123, 124
Ts	KH / $(R_2N)_2Cu(CN)Li_2$	NR_2	123, 124
Ts	KH / $(Me_3Sn)_2Cu(CN)Li_2$	$SnMe_3$	123, 124
Ts	KH / $(Me_3Si)_2Cu(CN)Li_2$	$SiMe_3$	123, 124
Ts	KH / RSH	SR	123, 124

When the nitrogen is activated as a sulfonate, treatment with potassium hydride in aprotic media drives the equilibrium "in reverse" toward the oxirane form, and opening by a variety of cuprate reagents occurs, as for epoxy alcohols, at the less substituted position.[25, 123, 124]

Rearrangement and Opening in Thia-Payne Systems

The scope and limitations of thia-Payne rearrangements have been little explored. Conditions used for rearrangement of epoxy sulfides to thiiranium salts with in situ opening are summarized in Equation 45. Note that, as discussed above, some aluminum reagents open the resultant thiiranium salt selectively at C-2.



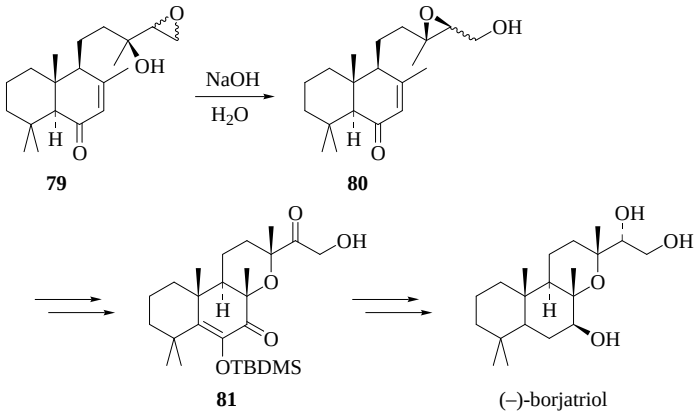
(Eq. 45)

Rearrangement/Opening Reagents	X	Major Product	refs
(*i*-Bu)$_2$AlH	H	**I**	67
Me_3Al	Me	**II**	67
Et_3Al	Et	**II**	67
$Et_2AlC{\equiv}CBu$-*t*	C≡CBu-*t*	**I**	67
$Me_2AlC{\equiv}CTMS$	C≡CTMS	**II**	68
$PhB(OH)_2$	OH	**I**	69
BF_3•Et_2O / R_2NTMS	NR_2	**I**	66, 125
TMSOTf / RNH_2	NHR	**I**	126, 127
TMSOTf / RN=CHR'	NHR	**I**	66, 128
TMSOTf / TMS-imidazole	imidazolyl	**I**	66, 125
TMSOTf / pyridine	py^+	**I**	66
TMSOTf / (*O*)-TMS amide enolate	NHAc, NRAc	**I**	66, 125
TMSOTf / PhSTMS	SPh	**I**	129

APPLICATIONS TO SYNTHESIS

Epoxide Migration in Acyclic Systems

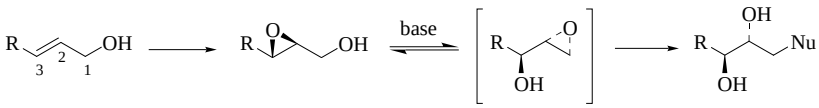
Epoxide Migration Prior to Opening ("Payne Rearrangement Method"). A rare example of the isolation of an epoxide migration product in a natural product synthesis is found in the synthesis of (−)-borjatriol (Scheme XII).[130] A key transformation involves Payne rearrangement of epoxy alcohol mixture **79** to **80**. Without separation, this mixture was carried through to ketone **81**, which was ultimately converted into the target compound.



79 **80** **81**

Scheme XII

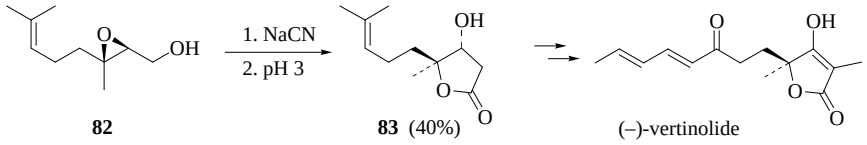
Nucleophilic Opening in situ ("Payne Rearrangement/Opening Method"). One common use of epoxide migration in acyclic systems has been the transformation of an allylic alcohol into a 2,3-diol with addition of a nucleophile at C-1. The most direct route for this transformation is asymmetric epoxidation followed by epoxide migration with in situ nucleophilic opening (Scheme XIII).[4]



Scheme XIII

For example, asymmetric epoxidation of geraniol with L-(+)-diethyl tartrate gives epoxy alcohol **82** (Scheme XIV). Treatment of this compound with sodium

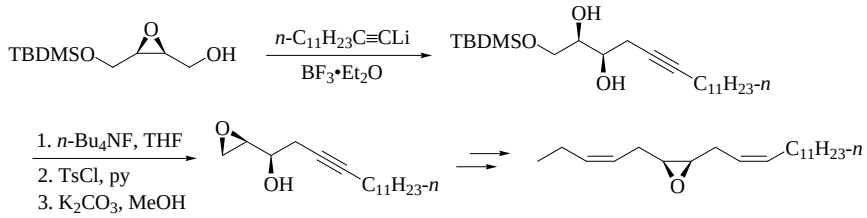
cyanide followed by mild acid hydrolysis leads to lactone **83**, an intermediate in the synthesis of (−)-vertinolide.[131]



82 **83** (40%)

Scheme XIV

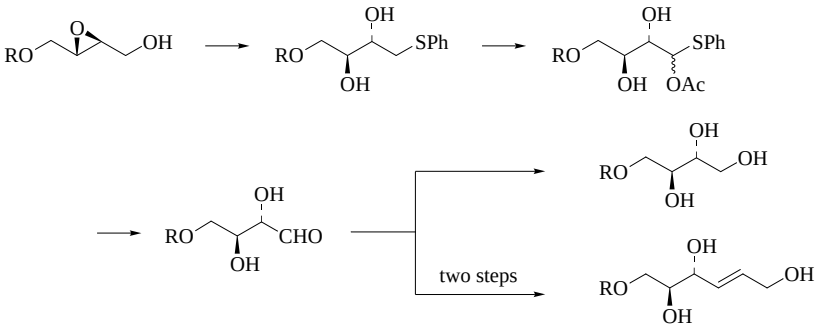
Although not particularly regioselective, in situ opening by alkynyllithium reagents in the presence of boron trifluoride etherate[89] has been used in the synthesis of lepidopteran pheromones (Scheme XV).[87] Even though regioselectivity was only 75 : 25 for C-1 vs. C-2 addition, Payne rearrangement/opening solved a difficult problem in this case, because the previously reported attempted synthesis of this class of compounds[132] using an alternative strategy was not successful.



Scheme XV

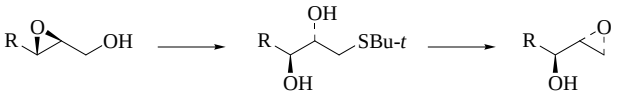
With hydroxide as the nucleophile, Payne rearrangement/opening has been used to synthesize all possible simple carbohydrate pentitols and hexitols[31] as well as a variety of 2-deoxyhexoses.[133] In all instances, regioselectivity for opening at C-1 is high because of the presence of an alkoxy substituent at C-4.

When the nucleophile is a thiolate, Payne rearrangement/opening is especially successful and has been used effectively in several natural product syntheses, including the syntheses of all possible simple tetritols[31] and hexoses.[99,134] Here the strategy (Scheme XVI) was to carry out a Pummerer reaction[135] on the resultant phenyl thioether to give the aldehyde. Reduction with lithium aluminum hydride produces the tetritol; Wittig reaction extends the carbohydrate backbone by two carbons and sets the stage for another asymmetric epoxidation in the synthesis of the hexoses.



Scheme XVI

Three-Step Equivalent Sequence ("Diol-Sulfide Method"). Epoxide migration and opening can be carried out in separate steps in cases where competition with C-3 opening is a problem or where the basic conditions necessary for epoxide migration are not compatible with the required nucleophile (Eq. 46).[91] In this method, the initial epoxide migration/opening is carried out using a *tert*-butylthiolate nucleophile. Treatment of the isolated thioether with trimethyloxonium tetrafluoroborate (Meerwein's reagent)[136] and displacement of *tert*-butyl methyl sulfide under aprotic basic conditions produces the *less favorable* epoxide migration product cleanly. This epoxide is then opened in a separate step using aprotic conditions, thus avoiding concurrent epoxide migration back to the energetically more favorable isomer.

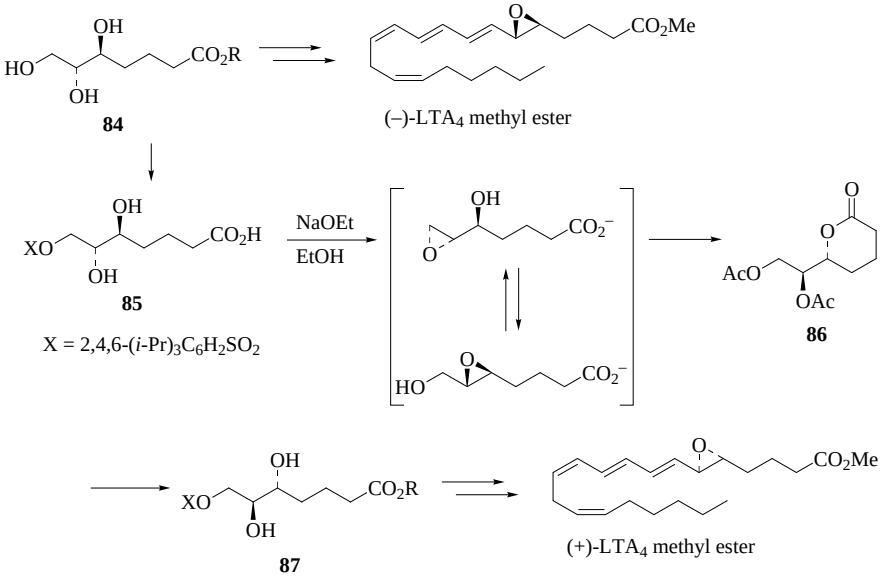


(Eq. 46)

The advantages of the diol-sulfide method over the direct Payne rearrangement are that the steps involved are generally all high yielding, and isolation of the less favorable epoxide prior to opening allows the use of a broader range of nucleophiles, including hydride, acetylide, cyanide, methylcuprate, and azide. Thus, this method provides the synthetic chemist with a "back-up plan" when direct in situ opening is found to be unsuitable.

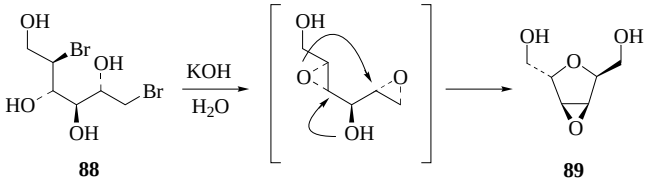
Intramolecularly Directed Chirality Inversion. A relatively unexploited use of epoxide migration in the synthesis of acyclic systems is based on the phenomenon that migration can lead to inversion of multiple stereocenters. Indeed, in certain cases, all of the centers of a molecule may be inverted if opening by hydroxide or a hydroxide equivalent is employed. Whereas the inversion of all of the stereocenters in a molecule may seem contrary to the goal of synthesis, in fact exactly this strategy has been used to good effect in at least one case.[34] Thus, both enantiomers of leukotriene A_4 methyl ester are available from the same starting compound (Scheme XVII). (−)-LTA_4 is available from triol **84** directly.[137] Alternatively, acti-

vation of triol **84** as the 2,4,6-triisopropylphenylsulfonate and hydrolysis gives acid **85**. Treatment of this acid with sodium ethoxide in strictly anhydrous ethanol (so as to prevent opening by hydroxide) followed by acetylation gives lactone **86**, with both stereocenters inverted, in 88% yield. Conversion into the activated ester **87** allows for the formal synthesis of (+)-LTA_4 methyl ester.



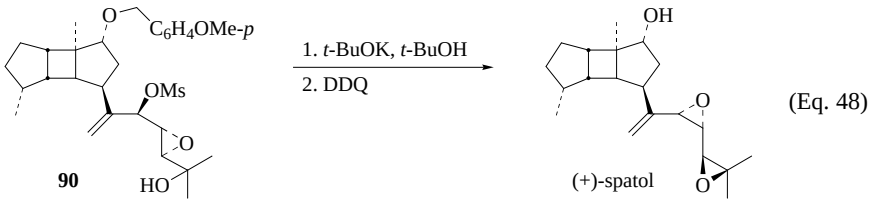
Scheme XVII

A second example involves the synthesis of tetrahydrofuran diol **89** from readily available dibromide **88** in 52% yield (Eq. 47).[45] Although not utilized to date in synthesis, this diol would seem to hold potential as a pseudo-C_2-symmetric ligand.[138,139] Note that the α- and β-epoxides are identical compounds.



(52%) (Eq. 47)

Epoxide Migration with Electrophilic Trapping in situ. The last two steps in the total synthesis of spatol illustrate the in situ electrophilic trapping of an epoxide migration product (Eq. 48). Treatment of mesylate **90** with potassium *tert*-butoxide in *tert*-butyl alcohol gives spatol after oxidative removal of the *p*-methoxybenzyl protecting group.[114]

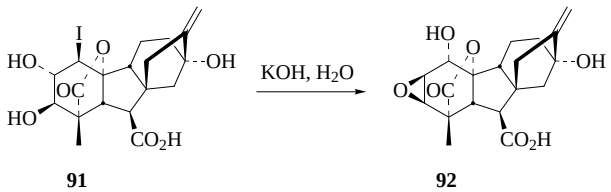


(Eq. 48)

Epoxide Migration in Cyclic Systems

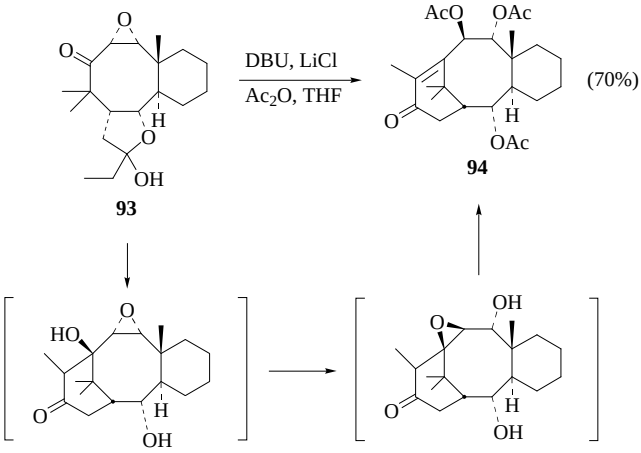
In the carbohydrate area, epoxide migration has not been used systematically except for the simple transformation of one known pyranose into another. Primary interest has been in understanding the chemistry of carbohydrates, with no specific synthetic goal in mind.

However, the lessons learned in the carbohydrate field have been applied to more complex syntheses. In particular, the preference for equatorial groups in pyranose systems was used in the synthesis of a derivative of gibberelin A_7 (Eq. 49). Upon treatment with base, iodohydrin **91** closes and rearranges to give migrated epoxy alcohol **92** in 63% yield.[140]



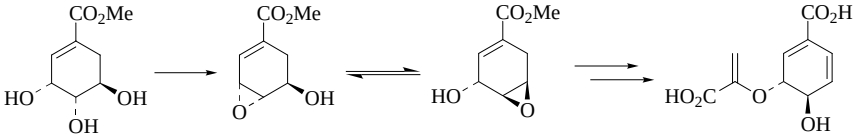
(63%) (Eq. 49)

In a model study for the synthesis of taxinine (Scheme XVIII), the transformation of epoxy ketone **93** into enone **94** has been proposed to take place via a tandem aldol/Payne rearrangement.[141] No intermediates were isolated, and exposure of epoxide **93** to base in the absence of acetic anhydride led only to decomposition.



Scheme XVIII

Unanticipated epoxide migration led to problems in the natural product isolation and surprises in the synthesis of epoxycyclohexenes **95** and **96** (Scheme XIX). These two compounds were not recognized to be distinct substances when isolated from the fungus *Chalara microspora*.[142] With almost identical 100 MHz NMR spectra, the presence of isomer **96** in the natural isolate was not initially noticed. However, when epoxide **95** was independently synthesized from (−)-methyl shikimate, it was discovered to have an unexpectedly high optical rotation.[143,144] It would appear that the natural isolate, with a rotation of +95°, was actually a 1:1 mixture of epoxy alcohols **95**, with a rotation of of +248°, and **96**, with a rotation of −54°.[145]



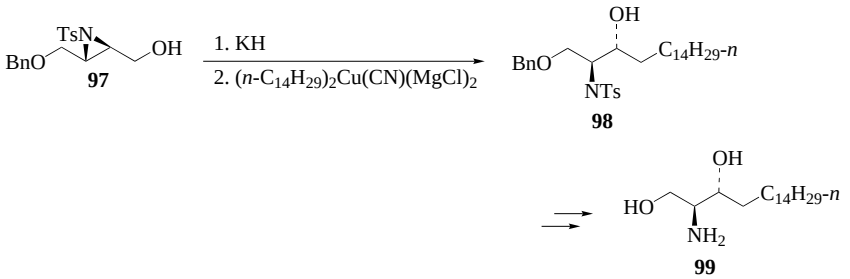
(–)-methylshikimate **95** **96** (–)-chorismic acid

Scheme XXI

In this instance, epoxide migration could be prevented by using cold sodium methoxide in methanol for the synthesis of isomer **95**. Use of sodium methoxide in methanol at room temperature generates a 25:75 ratio of **95** to **96**. Since isomer **96** has been converted into (−)-chorismic acid independently,[145] its preparation from (−)-methyl shikimate constitutes a formal synthesis of (−)-chorismic acid from (−)-methyl shikimate.

Aza-Payne and Thia-Payne Rearrangements

Aza-Payne and thia-Payne rearrangements are new enough discoveries that only a few applications to synthesis have been described, and these mainly involve simple demonstrations of the method. For example, aza-Payne rearrangement of aziridine **97** with in situ opening by a cuprate reagent gives intermediate **98** (Scheme XX), which was used in a synthesis of dihydrosphingosine (**99**).[123,124]

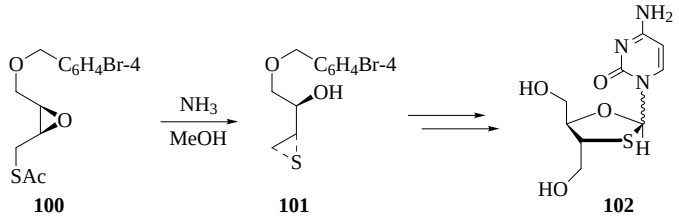


97 **98** **99**

Scheme XX

A recent application of the thia-Payne rearrangement has been reported. Thus, thia-Payne rearrangement of epoxide **100** (Scheme XXI) to thiirane **101** in 89%

yield allowed for the synthesis of the novel nucleoside **102**, which was investigated for HIV-1 inhibitory activity.[65]



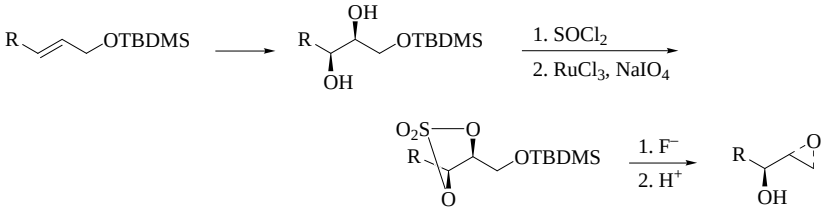
100 **101** **102**

Scheme XXI

COMPARISON WITH OTHER METHODS

Asymmetric Dihydroxylation Sequence I ("Cyclic Sulfate Method")

A method leading from allylic alcohols to 2,3-diols with nucleophilic opening at C-1 has been developed that involves 2,3-sulfates rather than 2,3-epoxides (Scheme XXII).[146,147]

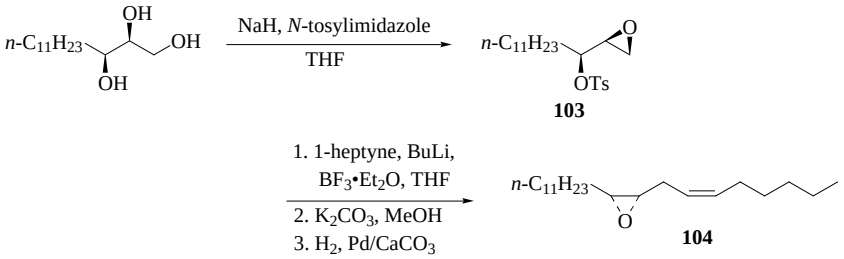


Scheme XXII

This sequence begins with the initial asymmetric dihydroxylation[148–150] of an allylic silyl ether. Treatment of the resultant diol with sulfuryl chloride[151] or, preferably, thionyl chloride followed by oxidation[152,153] generates a cyclic sulfate. This sulfate, when treated with fluoride in a nearly anhydrous solution followed by acidic hydrolysis, generates a terminal epoxide identical to that achieved by asymmetric epoxidation and epoxide migration. The cyclic sulfonate method has the advantage of avoiding the strongly basic conditions required for epoxide migration.

Asymmetric Dihydroxylation Sequence II ("C-3 Sulfonate Method")

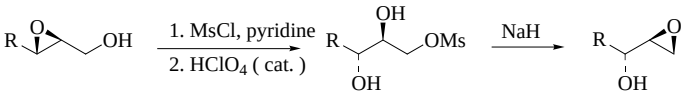
A second alternative method involving asymmetric dihydroxylation has been developed in the area of pheromone synthesis (Scheme XXIII).[154] In this method, the triol from asymmetric dihydroxylation of an allylic alcohol is treated with sodium hydride and *N*-tosylimidazole[155] to provide the 1,2-epoxy-3-tosylate **103** directly. Coupling of this compound with an alkynyllithium reagent, treatment with potassium carbonate, and hydrogenation gives the target pheromone **104**.



Scheme XXIII

C-2 Stereochemical Retention Sequence I ("Diol-Sulfonate Method")

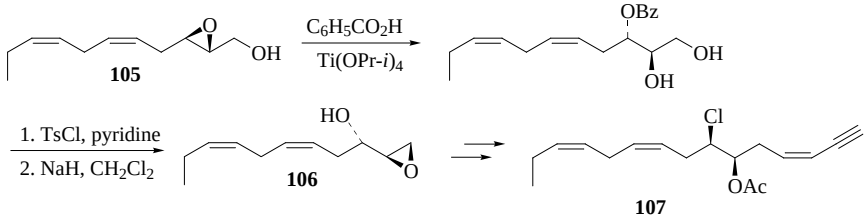
Treatment of a 2,3-epoxy alcohol with an alkyl- or arylsulfonyl chloride followed by acid-catalyzed C-3 opening and sulfonate displacement using base (Eq. 50) is an alternative method of transposing epoxy alcohol functionality.[91] There is no inversion at C-2, and an epoxy alcohol of opposite relative configuration to that of epoxide migration is obtained.



(Eq. 50)

C-2 Stereochemical Retention Sequence II (Titanium-Mediated Opening)

A second method of transposing epoxy alcohol functionality without inversion at C-2 involves initial treatment of the product of asymmetric epoxidation with benzoic acid in the presence of titanium(IV) isopropoxide,[156] followed by C-1-selective sulfonylation and displacement.[157] For example, in the synthesis of laurediol-related polyene **107** (Scheme XXIV), epoxy alcohol **105** is converted into epoxy alcohol **106** in 60% yield by treatment with benzoic acid in the presence of titanium(IV) isopropoxide followed by tosylation and displacement.[158] Note that in this method, as in the diol-sulfonate method, it is C-3 that is inverted, not C-2.

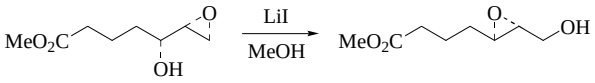


Scheme XXIV

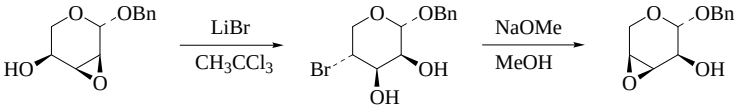
C-2 Stereochemical Retention Sequence III (Lithium Salt Induced Double Inversion)

Several intriguing reports suggest that lithium salts can be used to transpose epoxy alcohol functionality without inversion at C-2 in only one or two steps. Treat-

ment of epoxy alcohol **108** (Eq. 51) with lithium iodide in hot methanol gives rearranged epoxy alcohol **109** in 50% isolated yield, presumably by iodide addition at C-2 followed by displacement by the C-3 hydroxyl.[159] Similarly, treatment of 2,3-anhydropyranoside **110** (Eq. 52) with lithium bromide in refluxing 1,1,1-trichloroethane (which acts as a proton source for lithium alkoxides) gives bromodiol **111**, the product of opening at C-3 (pyranose numbering), displacement by the C-4 hydroxyl, and opening again at C-4. Treatment of this bromodiol with sodium methoxide gives the rearranged 3,4-anhydropyranoside **112** in 40% overall yield.[160]

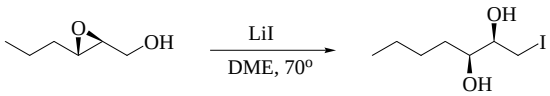


108 **109** (Eq. 51)



110 **111** **112** (Eq. 52)

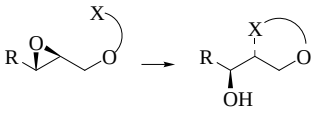
A similarly intriguing result involves the treatment of *trans*-2,3-epoxy alcohols with lithium iodide in hot dimethoxyethane, which results, effectively, in the *reverse* of Eq. 52. A product analogous to **111** is isolated in moderate yield (Eq. 53).[161] Although the yields in these transformations, typically 65–85%, are not especially high, one must marvel at the complexity of the reaction, which almost certainly involves reversible addition of iodide at all three possible positions, C-1, C-2, and C-3. Ultimately, thermodynamic control leads to a preponderance of the primary iodide. The corresponding *cis*-2,3-epoxy alcohols are equally good substrates, and the product iododiols are excellent substrates for reduction, alkylation, and cuprate coupling reactions at C-1.[162]



(65%) (Eq. 53)

C-1-Directed C-2 Opening (Neighboring Group Assistance)

Finally, a strategy that effects the transformation of a 2,3-epoxy alcohol into a 1,3-diol with nucleophilic opening at C-2 is outlined in Eq. 54. Though outside the scope of this chapter and reviewed elsewhere,[13] this strategy is mentioned here as an alternative to epoxide migration.



(Eq. 54)

Examples include X=O using carbamates,[163–165] carbonates,[166] acetals,[167,168] X=N using carbamates,[169] *N*-acylcarbamates,[170] and acetimidates,[171] and X=S using xanthates.[172,173] C-1-Directed opening of cyclic sulfates has also been demonstrated,[174,175] but as yet has been little explored.

EXPERIMENTAL CONDITIONS

Epoxide Migration Without Opening

The classic conditions for epoxide migration are treatment of an epoxy alcohol or epoxy alcohol precursor with either aqueous barium hydroxide[2,77] or sodium hydroxide[3] at room temperature. In the case of barium hydroxide, reactions are allowed to proceed for several hours; with sodium hydroxide, reactions are generally complete within 1 hour.[176] However, in many of these historically interesting examples yields are either low or not determined, and many represent crystallizations from complex mixtures. It is almost certain that substantial opening by hydroxide occurred. It now appears that the best way to effect epoxide migration without adventitious opening by hydroxide is the use of strictly anhydrous protic conditions such as freshly prepared sodium methoxide in methanol.[33,34,54,177] Under these conditions migration is slower, and reactions typically run for at least 24 hours.

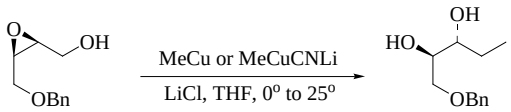
Other protic conditions that have been reported to be effective in specific cases include sodium sulfite[178] or potassium hydroxide[52,179] in aqueous methanol, sodium hydroxide in acetone or *tert*-butyl alcohol,[73] lithium hydroxide in a two-phase water/ether system,[180] potassium *tert*-butoxide in *tert*-butyl alcohol,[181] potassium carbonate in hot isopropyl alcohol,[182] and brief treatment with room-temperature[32] or hot[183] aqueous potassium hydroxide.

Despite the fact that aprotic conditions were first reported to not effect epoxide migration,[3] several successful epoxide migrations utilizing aprotic bases have been reported. Conditions include sodium, potassium, or calcium hydride in tetrahydrofuran,[184] potassium *tert*-butoxide in dimethyl formamide,[185] and lithium diisopropyl amide[84] or *tert*-butyllithium[186] in tetrahydrofuran at $-78°$. In the case of *tert*-butyllithium, the system was sufficiently substituted that nucleophilic opening was strongly disfavored.

Epoxide Migration With Nucleophilic Opening in situ

When in situ epoxide opening is desired, optimal conditions depend strongly on the nucleophile. Hydride addition has been effected using sodium borohydride in refluxing water/*tert*-butyl alcohol mixtures with only moderate yields and selectivity.[4] Lithium aluminum hydride in tetrahydrofuran has also been used in isolated cases.[84,104] Cyanide addition has been accomplished in 30–60% yield using sodium cyanide in hot aqueous alcohol.[4,85,86,131,187] A variety of conditions for cuprate additions are tabulated in Table III-B.

In a detailed study of conditions for alkyl addition to *cis*-4-benzyloxy-2,3-epoxy-1-butanol (**113**, Eq. 55), it was found that addition of lithium chloride enhances epoxide migration and leads to high yields and selectivities.[25,90] For example, addition of methylcopper or lithium methyl(cyano)cuprate to epoxy alcohol **113** gives diol **114** in high yield only when lithium chloride is present. Reaction without lithium chloride or the use of more reactive cuprate reagents results in nonselective opening.



113 **114** (>90%) (Eq. 55)

High yield and selectivity for the addition of azide to epoxy alcohol **113** result from using sodium azide in acetonitrile in the presence of lithium perchlorate.[93] Epoxide migration upon direct addition of amines has been attempted with only moderate success, as indicated in Table III-C, with yields of selected isomers ranging from 30–60%.

Where hydroxide addition is desired, use of excess aqueous potassium hydroxide and pH above 14 has been recommended.[14] Many studies have employed sodium, potassium, or lithium hydroxide in water or water/organic solvent mixtures, and most involve heating to 70–100°. Thiol addition has been carried out almost exclusively with thiophenol[31,38,99] or *tert*-butylthiol[91] in the presence of sodium hydroxide in aqueous *tert*-butyl alcohol or 1,4-dioxane. Heating is generally required.

Epoxide Migration With Electrophilic Trapping in situ

Conditions for in situ electrophilic trapping of epoxy alcohols after epoxide migration have generally been standard conditions for epoxide migration: aqueous hydroxide[115,188] or alcoholic potassium *tert*-butoxide.[114] However, as mentioned above (Eqs. 36–38), trapping of a primary alcohol over a tertiary one has been reported using allyl or benzyl bromide with sodium hydride in tetrahydrofuran,[112] and trapping of a secondary over a tertiary alcohol has been accomplished upon silylation.[113]

Aza-Payne Rearrangement

Forward Aza-Payne Rearrangement of 2,3-Epoxy Amines. Two reported procedures appear to be useful for the general transformation of a 2,3-epoxy amine into a 2-aziridinemethanol. Butyllithium/potassium *tert*-butoxide[58] in tetrahydrofuran at −78° is effective,[57] as is trimethylaluminum added to the lithium salt of the 2,3-epoxy amine (prepared by treatment of the 2,3-epoxy amine with butyllithium).[61] In cases where both methods have been used on the same substrate, butyllithium/potassium *tert*-butoxide appears to give slightly better yields.

Forward Aza-Payne Rearrangement of *N*-Tosyl Epoxy Amines.[63] These transformations, only possible for highly biased substrates (*i.e.* tertiary sulfonamides), are carried out under typical epoxide migration conditions, namely 5%

aqueous sodium hydroxide solution at room temperature or warmed briefly to reflux.

Reverse Aza-Payne Rearrangement of *N*-Tosyl-2-aziridinemethanols.[57] The formation of an *N*-tosyl-2,3-epoxy amine from an *N*-tosyl-2-aziridinemethanol is best carried out using potassium hydride or sodium hydride in tetrahydrofuran or a mixture of tetrahydrofuran and hexamethylphosphoric triamide at reduced temperature. Yields are typically high, in the range 80–99%.

Forward Aza-Payne Rearrangement of 2,3-Epoxy Amines with Opening in situ.[62] These reactions, using tertiary amine substrates, are performed using trimethylsilyl trifluoromethanesulfonate in dichloromethane at −78°. The epoxy amine is treated with the sulfonate for just a few minutes, then the nucleophile is added and the reaction is allowed to warm to room temperature and stirred for up to several days. Yields in the range 60–90% are typical.

Reverse Aza-Payne Rearrangement of *N*-Tosylaziridinemethanols with Addition in situ.[124] These reactions, effective with a wide variety of cuprate reagents of the type $XCu(CN)Li \cdot LiBr$ or $X_2Cu(CN)Li_2$, are carried out in two steps. First the substrate is deprotonated in THF at −78° and allowed to warm to 0°. Then the reaction mixture is cooled again to −78° and treated with five equivalents of the cuprate reagent. Early procedures involving cuprate reagents directly without initial deprotonation by potassium hydride[57,64] are no longer recommended.[20,123,124] Use of a higher-order cuprate reagent is critical; methyllithium and methylmagnesium bromide have been found to lead to complicated mixtures of products. For addition of cyanide, ytterbium cyanide/trimethylsilyl cyanide[189,190] is effective. Yields are typically in the 80–95% range.

Thia-Payne Rearrangement

Thia-Payne Rearrangement of Epoxy Sulfides with Nucleophilic Opening at C-1 in situ. These reactions are carried out much the same as for the forward aza-Payne rearrangement of 2,3-epoxy amines, with in situ opening using trimethylsilyl triflate at low temperature.[66,126,127] Boron trifluoride etherate is an alternative Lewis acid for this transformation.[66,125] Yields are typically in the range 50–80%. Reduction and acetylide addition using aluminum reagents involves treatment with two equivalents of reagent at 0° in hexane.[67]

Thia-Payne Rearrangement of Epoxy Sulfides with Nucleophilic Opening at C-2 in situ. As mentioned above, recent reports indicate that trimethylaluminum (Eq. 17),[67] dimethyl(trimethylsilylethynyl)aluminum,[68] and phenylborinic acid (Eq. 19)[69] all react with 2,3-epoxy sulfides with opening at C-2. In the case of the aluminum reagent, reactions are carried out using two or three equivalents of reagent at 0° in hexane[67] or at −78° in dichloromethane.[68] Phenylborinic acid reactions are carried out with heating.

Prevention of Epoxide Migration

Over forty references to epoxide migration in the literature specifically describe substrates and conditions for which the reaction does *not* occur. In addition, over twenty of the cited examples in Tables I through IV are references to epoxide

migrations as an unwanted side reaction. These numbers suggest that a brief discussion of the means available to prevent epoxide migration is in order. Table VII lists all substrates and associated conditions for which it was deemed by the original authors significant or unusual enough to relate their negative results. Many of these reactions (or nonreactions, as the case may be) are related to successful epoxide migrations of the same or similar substrate, and all of the tables have been cross-referenced for purposes of comparison.

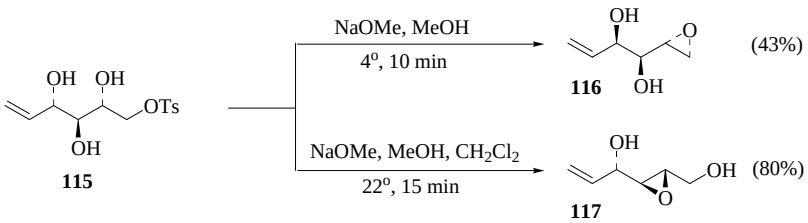
Payne's study clearly showed that epoxide migration does not generally occur when the base used is sodium hydride in tetrahydrofuran.[3] What becomes clear from these additional reports is that weakly basic conditions, particularly amine or carbonate bases in tetrahydrofuran, methanol or water, rarely lead to rearrangement and can often be utilized to effect other changes in the system without effecting epoxide migration. Both aqueous potassium carbonate[32,191,192] and aqueous ammonia[43,44] have been shown to effect epoxide opening without migration.

In the context of asymmetric epoxidation of acyclic allylic alcohols, epoxide migration was identified as a problem in the initial communication.[15] The difficulty arose from the strongly basic conditions used to hydrolyze the full equivalent of tartrate ester used in the reaction. However, with the use of distillation in the isolation of low molecular weight epoxy alcohols such as glycidol[193] and 4,5-epoxypent-1-en-3-ol (**11**, Scheme VI),[37,106] and the discovery that inclusion of molecular sieves in the reaction mix allows the use of a ten- to twenty-fold decrease in the amount of tartrate ester,[16,107,194] the problem of epoxide migration in asymmetric epoxidation can now be largely avoided.

For carbohydrates, epoxide migration typically occurs upon formation of the epoxide from a 1,2-*trans*-hydroxy tosylate. Migration can be avoided completely if the base used for ring closure is the basic form of Amberlite 400 resin,[195] or if the addition of base is done slowly at high temperature.[74]

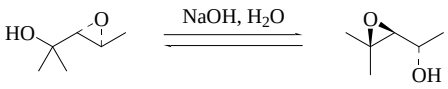
In terms of hydroxy protection, formyl groups[196] can be removed, and silylation,[196] acetylation,[53] tritylation,[53] benzylation,[197] and Mitsunobu inversion[165,198, 199] can all be accomplished without migration.

Temperature can also be a critical factor in preventing epoxide migration.[53,144] For example, with tosylate **115**, treatment with sodium methoxide (Scheme XXV) at low temperature produces unrearranged epoxide **116**, while treatment at room temperature produces the product of epoxide migration (**117**).[200]

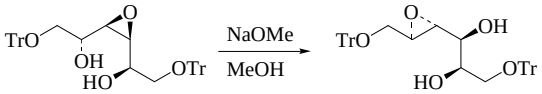


Scheme XXV

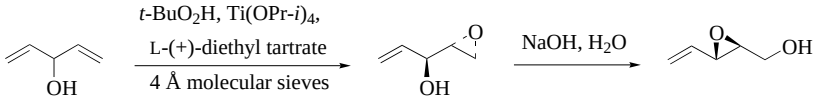
EXPERIMENTAL PROCEDURES



(±)-*trans*-2-Methyl-3,4-epoxy-2-pentanol and (2*RS*,3*RS*)-4-Methyl-3,4-epoxypentan-2-ol (Epoxide Migration Using Aqueous Sodium Hydroxide).[3] To 150 mL of 0.5 M aqueous sodium hydroxide previously cooled to about 5° was added 32.8 g (0.28 mol) of (±)-*trans*-2-methyl-3,4-epoxypentan-2-ol. The solution was allowed to warm to room temperature and remain there for 1 hour. After saturation with 100 g of ammonium sulfate, the solution was extracted with three 50-mL portions of chloroform. The combined chloroform extracts were washed with 25 mL of half-saturated aqueous ammonium sulfate, dried over magnesium sulfate, and concentrated on the steam bath to an internal temperature of 80−85°. Gas chromatographic analysis of the concentrate was made by means of a 2.5-m column packed with DC-710 on Fluoropak 80. The temperature was 100°, and a flow rate of 60 mL/min of helium was used. Emergence times of 9 and 15 minutes, respectively, were observed for the starting material (45%) and its isomer, (2*RS*,3*RS*)-4-methyl-3,4-epoxypentan-2-ol (55%).



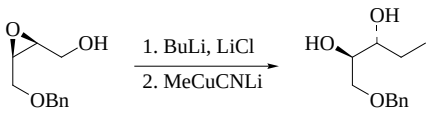
2,3-Anhydro-1,6-di-*O*-trityl-D-iditol (Epoxide Migration Using Sodium Methoxide in Methanol).[54] To 25 mL of 0.2 M sodium methoxide in methanol was added 2.5 g (3.9 mmol) of 3,4-anhydro-1,6-di-*O*-trityl-D-altritol. After 18 hours at room temperature, the solution was heated to reflux for 1 hour. The products were examined by TLC using Kieselgel G that had been spread as a slurry with 2% boric acid. Water (30 mL) was added to the solution, and the product was isolated by extraction with chloroform. The resulting syrup (2.3 g) was crystallized from aqueous methanol to give 2.1 g of the title compound (84%), mp 85°; $[\alpha]_D$ +10.0° (*c* 10.1, $CHCl_3$).



(2*S*,3*S*)-2,3-Epoxy-4-penten-1-ol (Asymmetric Epoxidation with Epoxide Migration in situ).[37,201] A mixture containing 15 g of activated powdered 4 Å molecular sieves in 450 mL of dichloromethane was cooled to −10°. To this vigorously stirred mixture was added 7.35 g (35.6 mmol) of L-(+)-diethyl tartrate and 8.44 g (29.7 mmol) of titanium(IV) isopropoxide. After cooling to −35°, the mixture was

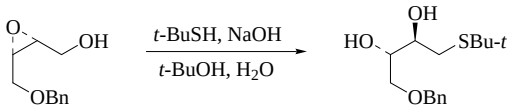
treated with 200 mL of a solution of *tert*-butyl hydroperoxide in dichloromethane (2.05 M, 410 mmol). After an additional 30 minutes stirring at −35°, a solution of 25.0 g (297 mmol) of divinylcarbinol in 20 mL of dichloromethane was added slowly over the course of 1 hour. After 7 days at −27°, the cold reaction mixture was slowly treated with 90 mL of a 16% w/w solution of acetic acid in water. The molecular sieves were removed by filtration, and the organic phase was removed and combined with five 40-mL dichloromethane extractions of the aqueous phase. After drying over sodium sulfate, the combined organic phases were concentrated and distilled in a 30-cm Vigreux column at water asprirator pressure (21 mmHg) to give 22.1 g of a colorless liquid, which by NMR spectroscopy was found to be 92% (3*S*,4*R*)-4,5-epoxy-1-penten-3-ol (the product of asymmetric epoxidation without epoxide migration) and 8% of a mixture of *tert*-butyl alcohol and *tert*-butyl hydroperoxide.

A solution of 2.10 g of a crude mixture prepared as described above (containing 19.9 mmol of unrearranged epoxy alcohol) in 30 mL of 0.5 M aqueous sodium hydroxide was stirred at room temperature for 45 minutes. After neutralization to pH 8 with ammonium chloride, the mixture was extracted four times with 30 mL of chloroform, and the combined organic phases were dried over sodium sulfate. Evaporation of solvent and Kugelrohr distillation (90–100°, 20 mmHg) provided a mixture containing 1.69 g of the title compound (85%) along with approximately 0.06 g of (3*S*,4*R*)-4,5-epoxy-1-penten-3-ol (3%), and 0.10 g of a mixture of *tert*-butyl hydroperoxide and *tert*- butyl alcohol; $[\alpha]_D$ −54.0° (*c* 1.43, $CHCl_3$); IR (neat) 3600–3300, 3090, 2990, 2920, 2870 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.08 (dd, $J = 2.3, 1.7$ Hz, 1 H), 3.29 (br, 1 H), 3.39 (dddd, $J = 7.5, 1.7, 1.5, 1.5$ Hz, 1 H), 3.66 (dd, $J = 12.5, 4.5$ Hz, 1 H), 3.92 (dd, $J = 12.5, 2.3$ Hz, 1 H), 5.31 (ddd, $J = 10.0, 1.5, 1.0$ Hz, 1 H), 5.49 (ddd, $J = 17.5, 1.5, 1.0$ Hz, 1 H), 5.61 (ddd, $J = 17.5, 10.0, 7.5$ Hz, (1 H).

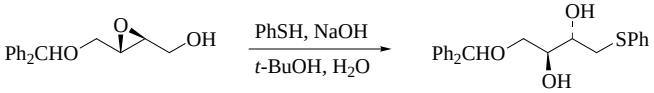


(2*RS*,3*RS*)-1-Benzyloxy-2,3-pentanediol (Epoxide Migration with Cuprate Addition in situ).[25] A solution of methyl(cyano)cuprate (Solution A) was prepared as follows: to a suspension of 0.35 g (3.91 mmol) of copper(I) cyanide in 5 mL of tetrahydrofuran under argon at 0° was added dropwise over about 5 minutes 2.76 mL of a solution of methyllithium in ethyl ether (1.4 M, 3.86 mmol). The colorless solution was stirred for 10 minutes at 0°, warmed to 25° over 30 minutes, then cooled again to 0°. Separately, a solution of the lithium salt of (±)-*cis*-4-benzyloxy-2,3-epoxy-1-butanol (Solution B) was prepared as follows: to a solution of 0.5 g (2.58 mmol) of the epoxy alcohol and 0.90 g (21.4 mmol) of lithium chloride in 10 mL of tetrahydrofuran under argon at −78° was added dropwise 1.65 mL of a solution of *n*-butyllithium in hexane (1.56 M, 2.58 mmol). The solution was stirred for 5 minutes at −78°, allowed to warm to 0°, and then stirred at that temperature for 10 minutes. The reaction was effected by the addition of Solution A to Solution B

via cannula at 0° followed by warming to room temperature over 2 hours. The reaction mixture was then stirred for a further 12 hours and then cautiously treated with 5 mL of saturated aqueous ammonium chloride. The mixture was stirred for 1–2 hours to aid removal of copper residues. Ethyl ether (20 mL) was then added, and the organic layer was separated. The aqueous phase was extracted twice with 20 mL of ethyl ether, and the combined organic phases were dried over magnesium sulfate, filtered, and concentrated to give 0.51 g of the title compound as a colorless oil (95%), IR (film) 3400, 3100, 3060, 3030, 2970, 2930, 2870, 1600, 1500, 1465, 1445, 1385, 1370, 1320, 1285, 1210, 1180, 1120, 1100, 1075, 1030, 1020, 980, 905, 830, 750, 730, 710, 695 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.90 (t, J = 6.0 Hz, 3 H), 1.37–1.53 (m, 2 H), 3.20 (br s, 2 H), 3.40–3.65 (m, 4 H), 4.48 (s, 2 H), 7.29 (s, 5 H).

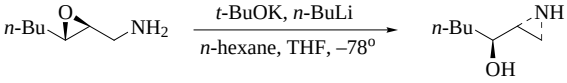


(2*S*,3*R*)-1-Benzyloxy-4-*tert*-butylthio-2,3-butanediol (Epoxide Migration with Nucleophilic Opening in situ by *tert*-Butyl Thiol).[91] The solvents required for this reaction were deoxygenated prior to use by the rapid passage of nitrogen through the solvent for not less than 30 minutes. A solution of 3.02 g (1.56 mmol) of (2*R*,3*S*)-4-benzyloxy-2,3-epoxy-1-butanol in 7.8 mL of *tert*-butyl alcohol and 7.8 mL of 0.5 M aqueous sodium hydroxide was immersed in a preheated oil bath at 70°. The reaction mixture was stirred vigorously as a dropwise addition of a solution of 0.176 g (0.220 mL, 1.96 mmol) of *tert*-butyl thiol in 2 mL of *tert*- butyl alcohol was conducted over a period of 40 minutes. During this time the oil bath temperature rose to 78°. Stirring was continued for 20 minutes after the dropwise addition was complete. The reaction mixture was then cooled to room temperature and neutralized with saturated aqueous ammonium chloride. Sufficient water was added to clarify the aqueous phase, and the phases were then separated. The aqueous phase was extracted five times with dichloromethane, and the combined organic phases were washed with saturated aqueous ammonium chloride, dried over sodium sulfate, concentrated, and the residue was dried under high vacuum. Flash chromatography gave 0.276 g of the title compound as an oil (62%), $[\alpha]_D$ −10.6° (*c* 1.98, $CHCl_3$); $[\alpha]_D$ +5.8 (*c* 0.80, EtOH); IR (NaCl) 3400, 3090, 3070, 3030, 2960, 2930, 2900, 2870, 1455, 1365, 1100, 740, 700 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.32 (s, 9 H), 2.61–2.85 (m, 3 H), 2.92 (d, J = 4.1 Hz, 1 H), 3.64 (m, 2 H), 3.81 (m, 1 H), 4.54, 4.58 (AB, J_{AB} = 12 Hz, 2 H), 7.25–7.41 (m, 5 H).

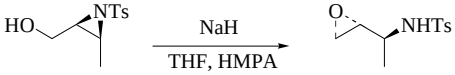


(2*S*,3*S*)-1-Benzhydryloxy-4-phenylthio-2,3-butanediol (Epoxide Migration with Nucleophilic Opening in situ by Thiophenol).[99] To a vigorously stirred

refluxing mixture of 8.075 g (29.87 mmol) of (2*S*,3*S*)-4-benzhydryloxy-2,3-epoxy-1-butanol in 150 mL of *tert*-butyl alcohol and 150 mL of 0.5 M aqueous sodium hydroxide was added via syringe over a period of 3 hours a solution of 4 mL (38.8 mmol) of thiophenol in 40 mL of *tert*-butyl alcohol. The reaction mixture was cooled to room temperature, and the two phases were separated. The organic phase was concentrated and diluted with 150 mL of dichoromethane, and the aqueous phase was extracted with portions of dichloromethane. The combined organic phases were washed successively with 1 M aqueous sodium hydroxide, water, and brine. Drying over sodium sulfate and concentration gave a crude solid, which was recrystallized from dichloromethane/hexane to give 8.070 g of the title compound as white needles (71%), mp 76–77.5°; $[\alpha]_D$ +43.4° (*c* 1.15, ethanol); IR (KBr) 3400, 2900 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.55 (d, $J = 5.1$ Hz, 1 H), 2.71 (d, $J = 4.1$ Hz, 1 H), 2.99 (dd, $J = 13.9$, 8.6 Hz, 1 H), 3.33 (dd, $J = 13.9$, 3.6 Hz, 1 H), 3.61 (dd, $J = 9.6$, 5.8 Hz, 1 H), 3.68 (dd, $J = 9.6$, 3.8 Hz, 1 H), 3.77–3.88 (m, 2 H), 5.38 (s, 1 H), 7.20–7.40 (m, 15 H).

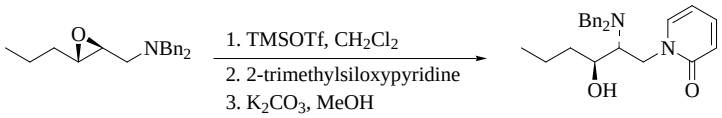


(2*R*,α*S*)-α-Butyl-2-aziridinemethanol. (Forward Aza-Payne Rearrangement of an Epoxy Amine Using Super Base[58]).[57] To a stirred solution of 505 mg (4.5 mmol) of potassium *tert*-butoxide in 5 mL of tetrahydrofuran under argon at −78° was added dropwise 2.76 mL of a solution of *n*-butyllithium in hexane (1.63 M, 4.5 mmol), and the mixture was stirred for 10 minutes. To this mixture was added with stirring a solution of 388 mg (3.0 mmol) of (2*S*,3*S*)-2,3-epoxyheptylamine in 3 mL of tetrahydrofuran. Stirring was continued for 90 minutes. With vigorous stirring, the reaction was quenched at −78° with 4 mL of saturated aqueous ammonium chloride . The inorganic salts were removed by filtration through Celite, and the Celite was washed twice with 40 mL of ethyl ether. The combined organic solutions were dried over magnesium sulfate and concentrated under reduced pressure to give 328 mg of the title compound as a colorless solid (85%). Recrystallization from ethyl ether/*n*-hexane (1:5) gave colorless crystals, mp 65°; $[\alpha]_D$ +39.9° (*c* 1.69, $CHCl_3$); IR ($CHCl_3$) 3450, 3330 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 0.92 (m, 3 H), 1.28–1.43 (m, 4 H), 1.45–1.57 (m, 3 H), 1.61 (d, $J = 3.6$ Hz, 1 H), 1.72 (d, $J = 5.9$ Hz, 1 H), 2.14 (ddd, $J = 5.9$, 3.6, 3.6 Hz, 1 H), 3.63 (m, 1 H).

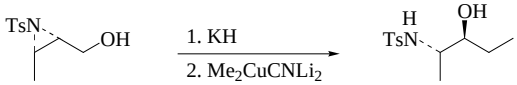


(2*S*,3*R*)-*N*-Tosyl-3,4-epoxy-2-butylamine (Reverse Aza-Payne Rearrangement of an *N*-Tosyl-2-aziridinemethanol Using Sodium Hydride).[57] To a stirred suspension of 24 mg (1 mmol) of sodium hydride in a mixture of 2 mL of tetrahydrofuran and 0.33 mL of hexamethylphosphoric triamide under argon at −40°

was added a solution of 60.3 mg (0.25 mmol) of (2*S*,3*S*)-3-methyl-1-tosyl-2-aziridinemethanol in 2 mL of tetrahydrofuran. The mixture was allowed to warm to room temperature, and stirring was continued for 2 hours. The reaction mixture was cooled to −78° and quenched with 2 mL of 5% aqueous citric acid with stirring. The mixture was extracted with ethyl acetate, and the extract was washed successively with saturated citric acid, brine, 5% aqueous sodium hydrogen carbonate, and brine. After drying over magnesium sulfate and concentration, flash chromatography (silica, 1:3 ethyl acetate/*n*-hexane) gave 56 mg of the title compound as a crystalline mass (92%). Crystallization from ethyl ether gave colorless crystals, mp 102–103°; $[\alpha]_D$ +9.9° (*c* 0.88, $CHCl_3$); IR ($CHCl_3$) 3385, 1602, 1335, 1152, 1092 cm^{-1}; ^1H NMR (300 MHz $CDCl_3$) δ 1.14 (d, J = 6.9 Hz, 3 H), 2.43 (s, 3 H), 2.69 (m, 2 H), 2.92 (m, 1 H), 3.60 (dddd, J = 15.5, 13.8, 6.9, 2.9 Hz, 1 H), 4.55 (d, J = 8.5 Hz, 1 H), 7.29–7.32 (m, 2 H), 7.73–7.82 (m, 2 H).

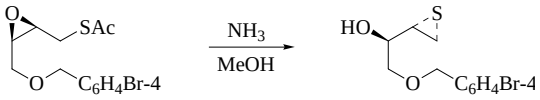


(2*RS*,3*SR*)-2-Dibenzylamino-1-(2-pyridon-1-yl)-3-hexanol (Aza-Payne Rearrangement of a Tertiary Epoxy Amine with in situ Nucleophilic Opening by an Amide Equivalent).[62] To a solution of 0.30 g (1.02 mmol) of (±)-*trans*-*N*,*N*-dibenzyl-2,3-epoxyhexylamine in 6 mL of dichloromethane under nitrogen at −78° was added 0.27 g (0.24 mL, 1.15 mmol) of trimethylsilyl trifluoromethanesulfonate. After 10 minutes, 0.34 g (2.04 mmol) of 2-trimethylsiloxypyridine was added, and the solution was allowed to warm to room temperature and stirred for 5 days. To the solution were added 9 mL of methanol and 0.80 g (5.8 mmol) of potassium carbonate, and the mixture was stirred an additional 12 hours. The solvent was removed in vacuo, and the residue was purified by column chromatography (flash silica, 85:15 ethyl acetate/petroleum ether) to give 0.37 g of the title compound as a colorless viscous oil (93%), IR (thin film) 3480–3180, 2940, 2900, 2880, 1650, 1570, 1540, 1450, 1245, 1140, 1065, 840, 750, 700 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.88 (t, J = 6.9 Hz, 3 H), 1.25–1.44 (m, 4 H), 2.91–2.92 (m, 1 H), 3.16 (d, J = 6.9 Hz, 1 H), 3.68 (d, J = 14.1 Hz, 2 H), 3.80 (dd, J = 13.5, 6.3 Hz, 1 H), 3.93 (d, J = 14.1 Hz, 2 H), 4.03–4.06 (m, 4H), 4.59 (dd, J = 13.5, 5.7 Hz, 1 H), 6.21 (t, J = 6.6 Hz, 1 H), 6.51 (d, J = 9.0 Hz, 1 H), 7.21–7.38 (m, 12 H) ; ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.02, 19.18, 38.46, 47.65, 54.56, 61.19, 69.79, 106.26, 120.84, 127.00, 128.33, 128.38, 138.78, 139.55, 163.14.

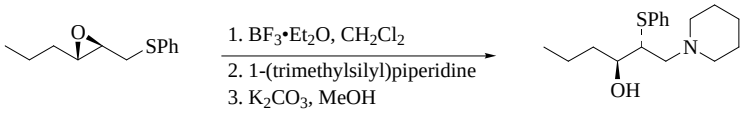


(2*S*,3*S*)-2-[(4-Methylphenyl)sulfonamido]-3-pentanol (Reverse Aza-Payne Rearrangement of an *N*-Tosyl-2-aziridinemethanol with Cuprate Addition in

situ).[124] To a stirred suspension of 40 mg (1 mmol) of potassium hydride in 2 mL of tetrahydrofuran under argon at −78° was added 121 mg (0.5 mmol) of (2*S*,3*S*)-3-methyl-1-tosyl-2-aziridinemethanol in 2 mL of tetrahydrofuran. The mixture was allowed to warm to 0°, and stirring was continued for 1 hour. To the mixture cooled to −78° was added by syringe 6 mL of a solution of $Me_2Cu(CN)Li_2 \cdot 2LiBr$ in a 1:1 mixture of tetrahydrofuran and ether (0.42 M, 2.5 mmol), prepared from 224 mg (2.5 mmol) of copper(I) cyanide and 3.3 mL of a solution of methyllithium/lithium bromide in ethyl ether (1.5 M, 5 mmol). The mixture was stirred at −78° for 30 minutes. With vigorous stirring at −78°, the reaction was quenched with 4 mL of a 1:1 mixture of saturated aqueous ammonium chloride and 28% aqueous ammonium hydroxide. The mixture was extracted with a 4:1 mixture of ethyl ether and dichloromethane. Evaporation, drying, and flash chromatography (silica, 1:2 ethyl acetate/*n*-hexane) gave 128 mg of the title compound as a crystalline mass (99%). Crystallization from ethyl ether/*n*-hexane (3:1) gave colorless crystals, mp 90°; $[\alpha]_D$ −3.3° (*c* 0.546, $CHCl_3$); IR ($CHCl_3$) 3550, 3400, 1598 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 0.88 (t, J = 7.4 Hz, 3 H), 1.02 (d, J = 6.6 Hz, 3 H), 1.44 (m, 2 H), 1.80 (br, 1 H), 2.43 (s, 3 H), 3.21–3.37 (m, 2 H), 4.78 (m, 1 H), 7.29–7.31 (m, 2 H), 7.75–7.79 (m, 2 H).



(2*R*,3*S*)-1-(4-Bromobenzyloxy)-3,4-epithio-2-butanol (Thia-Payne Rearrangement of an Epoxy Thioacetate).[65] To a solution of 4.60 g (13.9 mmol) of (2*R*,3*R*)-*S*-acetyl-4-[(4-bromobenzyl)oxy]-2,3-epoxy-1-butanethiol in 120 mL of methanol at 0° was added 12 mL of a saturated solution of ammonia in methanol. The reaction mixture was stirred at 0° for 3 hours, diluted with dichloromethane, washed with water, dried, filtered, and evaporated. Column chromatography (1:9 ethyl acetate/toluene) gave 3.57 g of the title compound as a colorless oil (89%), ^1H NMR (250 MHz, $CDCl_3$) δ 2.20 (d, J = 8.0 Hz, 1 H), 2.40 (dd, J = 5.6, 0.8 Hz, 1 H), 2.44 (dd, J = 6.5, 0.8 Hz, 1 H), 3.26 (ddd, J = 6.5, 5.6, 4.0 Hz, 1 H), 3.53 (dd, J = 9.5, 5.8 Hz, 1 H), 3.61 (dd, J = 9.5, 5.6 Hz, 1 H), 3.85 (ddd, J = 8.0, 5.7, 4.0 Hz, 1 H), 4.57 (s, 2 H), 7.2–7.5 (m, 4 H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 21.2, 38.1, 69.6, 72.8, 74.1, 121.7, 129.3, 131.6, 136.9.



(2*RS*,3*SR*)-2-Phenylthio-1-piperidino-3-hexanol (Thia-Payne Rearrangement of an Epoxy Sulfide with Nucleophilic Opening in situ Using a Silyl Amine).[66] To a solution of 100 mg (0.48 mmol) of (±)-*trans*-2,3-epoxyhexyl phenyl sulfide in 2 mL of dichloromethane at −78° was added 68 mg (0.48 mmol)

of trimethylsilyl trifluoromethanesulfonate. After 10 minutes, 76 mg (0.48 mmol) of 1-(trimethylsilyl)piperidine was added, and the solution was stirred for an additional 10 minutes at $-78°$. The solution was allowed to warm to 0° and stirred at that temperature overnight. Potassium carbonate (227 mg, 1.64 mmol) and 3 mL of methanol were added, and the mixture was stirred for 2 hours at room temperature. The mixture was concentrated, redissolved in 10 mL of dichloromethane, and washed twice with 2 mL of water. The aqueous washings were back-extracted four times with 5 mL of dichloromethane, and the combined dichloromethane solutions were dried over magnesium sulfate, filtered, and concentrated. Flash chromatography using 15 g of kieselgel and a 1:8:1191 mixture of aqueous ammonia (specific gravity 0.880), ethanol, and dichloromethane gave 56 mg of the title compound as a yellow oil (40%), IR (thin film) 3660–3040, 3080, 3060, 2960, 2940, 2860, 2820, 1580, 1480, 1460, 1440, 1380, 1350, 1310, 1270, 1190, 1155, 1135, 1110, 1090, 1070, 1040, 1030, 990, 965, 860, 740, 690 $cm^{-}1$; ^1H NMR (300 MHz, $CDCl_3$) δ 0.95 (t, $J = 7.0$ Hz, 3 H), 1.20–1.70 (m, 9 H), 1.90–2.03 (m, 1 H), 2.17–2.43 (m, 2 H), 2.43–2.67 (m, 2 H), 2.73 (AB, $\Delta v = 6.8$, $J = 10.4$ Hz, 2 H), 3.16 (dt, $J = 10.4$, 4.6 Hz, 1 H), 3.73 (dt, $J = 11.5$, 4.6 Hz, 1 H), 7.21–7.34 (m, 3H), 7.39 (d, $J = 7.5$ Hz, 2 H).

TABULAR SURVEY

Reactions involving epoxide migration are grouped in Tables I-IV. Aza-Payne rearrangements are presented in Tables V-A and V-B; thia-Payne rearrangements are collected in Table VI. Table VII is a collection of observations by authors specifically identifying substrates and conditions for which epoxide migration did not occur.

Tables I-A and I-B both present epoxide migrations in acyclic systems. Here *acyclic system* refers specifically to those structures for which the epoxide itself is not a part of a fused ring system in either isomer. Table I is separated into two parts: reactions where the substrate itself underwent the reaction (Table I-A) and reactions where the epoxy alcohol undergoing migration was generated in situ (Table I-B). Epoxide migration in *cyclic systems* (the epoxide is part of a fused ring system in one or both isomers) are similarly presented in Tables II-A and II-B.

In Tables I-A and II-A, the major isomer is tabulated in the first column and the minor in the second so as to allow a quick comparison of the effect of substituents on isomer ratio. Where one set of conditions favored one isomer and another set of conditions favored the other isomer, this organization requires two separate entries with switched major/minor isomers. The isomer ratios given here may or may not be true equilibrium ratios. In some cases they are simply ratios based on isolated yield.

Tables III-A through III-E present epoxide migrations which were followed by in situ nucleophilic addition. This includes reduction by hydride (Table III-A), addition of carbon-based nucleophiles including cuprates, acetylides, and cyanide (Table III-B), addition of nitrogen-based nucleophiles (amines, azide, and sulfonamides, Table III-C), addition of oxygen-based nucleophiles including hydroxide and alkoxides (Table III-D), and addition of thiols and halides (Table III-E).

Table IV presents epoxide migrations that involve in situ electrophilic trapping, either intra- or intermolecular.

Aza-Payne reactions are catalogued in Tables V-A (simple rearrangements) and V-B (rearrangement with in situ opening of the aziridine or aziridinium ion). In Table V-A the oxirane isomer is in the first column and given the designation **I**, while the aziridine isomer is in the second column as **II**. The starting isomer is then identified as either oxirane (**I**) or aziridine (**II**), and for the purposes of this chapter, "forward aza-Payne" reaction is thus from **I** to **II**.

Table VI presents all thia-Payne rearrangements reported to date. All start with the oxirane, all except one of which involve in situ opening of a presumed thiirane intermediate.

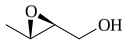
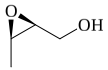
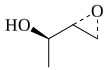
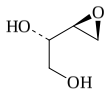
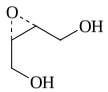
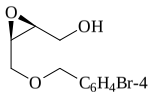
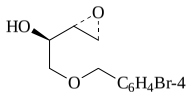
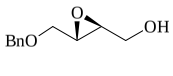
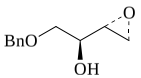
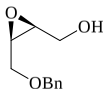
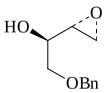
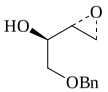
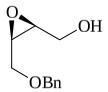
Table VII is somewhat of a departure from traditional *Organic Reactions* format in that it is a comprehensive collection of cases where the title reaction was specifically reported *not* to occur. This table is cross-referenced to the other tables to help the reader identify the sometimes subtle differences between successful and unsuccessful epoxide migration. It includes both reactions for which mild conditions allowed for synthetic transformations in the presence of a potentially migrating epoxide and reactions for which slight changes in substrate stereochemistry or regiochemistry led to surprisingly different epoxide behavior. Table VII does not include alicyclic systems bearing hydroxy and epoxide groups in a cis configuration, where migration is inherently impossible.

In all tables, entries are organized first by increasing number of carbons *in the contiguous carbon system containing the migrating heterocycle*, then by *total number of hydrogen atoms*. This organization was chosen so as to place related entries as close together as possible. Structural formulas have been normalized to emphasize the migration of interest. In particular, although many of the references are to the carbohydrate literature, all carbohydrates have been recast in a standard organic acyclic or alicyclic notation. The choice of this notation was made so as to allow a general overview of the reactions without a major distinction between carbohydrates and noncarbohydrates and to avoid two specific problems: the assumptions of conformation implicit in more standard carbohydrate notation and the odd sort of depiction required for representing *trans*-epoxides in Fischer projections. As much as possible, pyranose systems have been explicitly named so that those readers familiar with carbohydrate chemistry can make identifications quickly.

The following abbreviations are used in the tables:

(*R*,*R*)-**15**	See Eq. 8
Ac	acetyl
Bn	benzyl
Boc	*tert*-butoxycarbonyl
Bz	benzoyl
DBN	1,5-diazabicyclo[3.4.0]non-5-ene
DBU	1,8-diazabicyclo[5.4.0]undec-7-ene
DDQ	2,3-dichloro-5,6-dicyano-1,4-benzoquinone
DEAD	diethyl azodicarboxylate
DET	diethyl tartrate
DMAP	4-(dimethylamino)pyridine
DMF	dimethylformamide
DMSO	dimethyl sulfoxide
DMTS	dimethylthexylsilyl
EE	ethoxyethyl
HMPA	hexamethylphosphoric triamide
LDA	lithium diisopropylamide
Ms	methanesulfonyl
py	pyridine
TBDMS	*tert*-butyldimethylsilyl
TBDPS	*tert*-butyldiphenylsilyl
Tf	trifluoromethanesulfonyl
THF	tetrahydrofuran
THP	tetrahydropyranyl
TMS	trimethylsilyl
Tr	trityl
Ts	*p*-toluenesulfonyl

TABLE 1-A. EPOXIDE MIGRATION IN ACYCLIC SYSTEMS

	Major Isomer (**I**)	Minor Isomer (**II**)	Initial Isomer	Conditions	Final Mixture **I**:**II**	Final Mixture Yield (%)	Refs.
C_4			**I** or **II**	$NaOH, H_2O$, rt, 1 h	93:7	(—)	3
			I or **II**	"	90:10	(—)	42
			**I** or **II**	$NaOH, H_2O$, rt, 1 h	58:42	(—)[a]	3
			I or **II**	"	58:42	(—)	42
			**II**	(*R*,*R*)-**15** (1–2 mol%), CF_3CH_2OH, rt, 6 h	80:20	**I** (81)	55
			**I**	$NaOH, H_2O$, rt, 3 h	60:40	**II** (38)	65
			**II**	KOH, H_2O, THF, reflux, 1.5 h	90:10	(—)	30
			**I**	NaH, THF, 18-crown-6, 25°, 12 h	75:25	(—)	25
			I	BuLi, LiCl, THF, 25°, 4 h	70:30	(—)	25
			**I**	KOH, H_2O, THF, reflux, 2.5 h	50:50	(—)	30
			II	NaOH, H_2O, 25°, 1.5 h	54:46	(—)	25
			II	BuLi, LiCl (2 eq), THF, 25°, 12 h	60:40	(—)	25
			II	NaOH, H_2O, THF, reflux, 2 h	60:40	**I** (60)	202

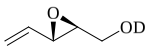
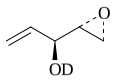
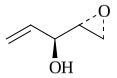
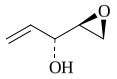
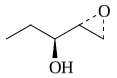
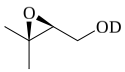
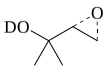
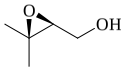
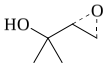
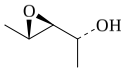
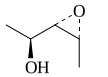
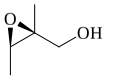
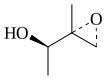
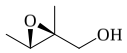
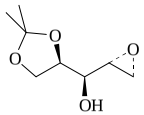
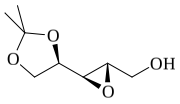
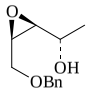
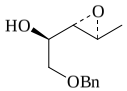
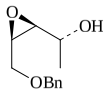
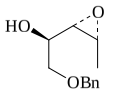
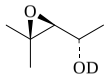
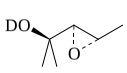
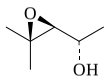
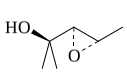
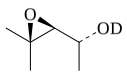
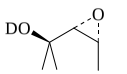
C_5			**II**	NaOD, D_2O, 0^o, 45 min	77:23 (—) 37
			II	NaOD, D_2O, 0^o, 2 h	90:10 (—) 37
			II	NaOD, D_2O, rt, 30 min	97:3 (—) 37
			**II**	NaOH, H_2O, rt, 30 min	97:3 (89)[a] 37
			**II**	NaOH, H_2O, -10^o	— **I** (89) 72
			**II**	NaOH, H_2O, 22^o, 1 h	90:10 (74) 71
			**II**	NaOD, D_2O	93:7 (—) 70
			**I** or **II**	NaOH, H_2O, rt, 1 h	92:8 (82)[a] 3
			I or **II**	"	90:10 (—) 42
			**I** or **II**	NaOH, H_2O, rt, 1 h	70:30 (—) 42
			**I** or **II**	NaOH, H_2O, rt, 1 h	65:35 (—) 42

TABLE 1-A. EPOXIDE MIGRATION IN ACYCLIC SYSTEMS (*Continued*)

Major Isomer (**I**)	Minor Isomer (**II**)	Initial Isomer	Conditions	Final Mixture **I**:**II**	Final Mixture Yield (%)	Refs.
		**I** or **II**	NaOH, H_2O, rt, 1 h	80:20	(—)	42
		**II**	NaOH, H_2O, *t*-BuOH	—	(—)	203
		**I**	NaH, THF, rt	77:23	(96)	26
		**I**	NaH, THF, rt	—	**I** (96)[a]	26
		**I**	NaOD, D_2O, rt, 1 h	52:48	(—)	70
		**I** or **II**	NaOH, H_2O, rt, 1 h	56:44	(—)	3
		I or **II**	"	56:44	(—)	42
		**I**	NaOD, D_2O, rt, 1 h	>95:5	(—)	70

C6

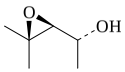
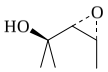
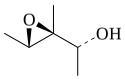
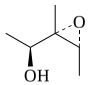
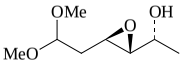
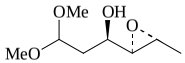
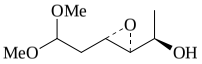
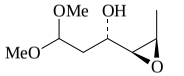
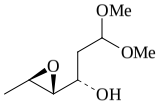
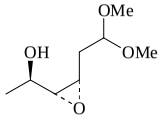
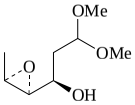
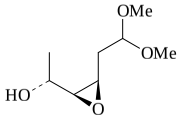
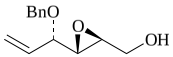
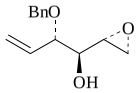
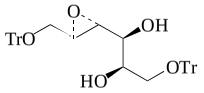
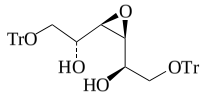
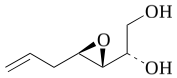
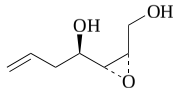
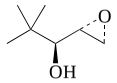
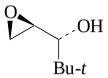
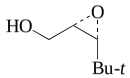
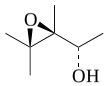
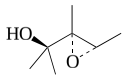
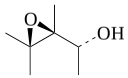
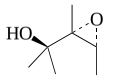
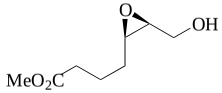
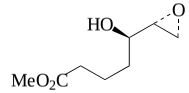
		**I** or **II**	NaOH, H_2O, rt, 1 h	95:5	(—)	3
		I or **II**	"	95:5	(—)	42
		**I**	NaOH, H_2O, rt, 1 h	88:12	(—)	42
		**I**	NaOH, H_2O, 20^o, 0.2 h	57:43	(—)	83
		**I**	NaOH, H_2O, 20^o, 0.2 h	90:10	(—)	83
		**II**	NaOH, H_2O, 20^o, 0.2 h	93:7	(—)	83
		**II**	NaOH, H_2O, 20^o, 0.2 h	55:45	(—)	83
		**II**	NaOH, H_2O, *t*-BuOH, 60^o, 45 min	—	**I** (69)	204

TABLE 1-A. EPOXIDE MIGRATION IN ACYCLIC SYSTEMS (*Continued*)

	Major Isomer (**I**)	Minor Isomer (**II**)	Initial Isomer	Conditions	Final Mixture **I**:**II**	Final Mixture Yield (%)	Refs.
			**II**	1. NaOMe, MeOH, rt, 18 h 2. reflux, 1 h	—	**I** (84)	54
C_7			**II**	NaOH, THF, rt	—	**I** (79)	133
			**I** or **II**	NaOH, H_2O, rt, 1 h	88:12	(—)	42
			**I** or **II**	NaOH, H_2O, rt, 1 h	95:5	(—)	42
			**I** or **II**	NaOH, H_2O, rt, 1 h	55:45	(—)	42
			**I** or **II**	NaOH, H_2O, rt, 1 h	93:7	(—)	42
			**II**	DBN, MeOH, 90°	—	**I** (20)	159

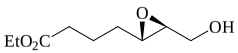
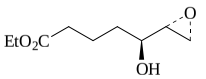
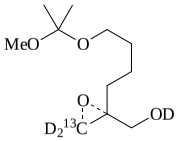
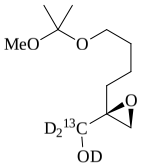
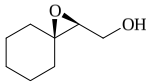
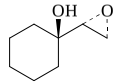
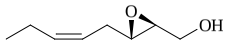
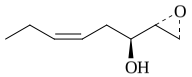
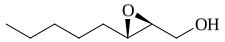
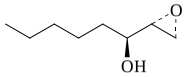
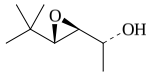
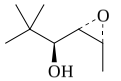
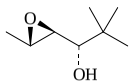
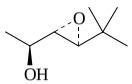
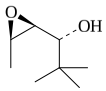
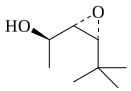
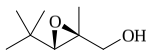
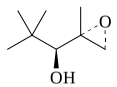
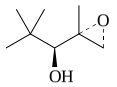
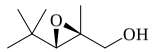
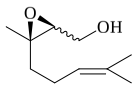
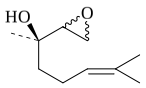
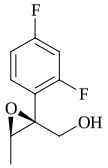
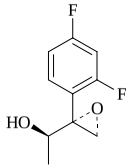
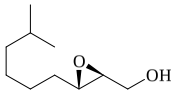
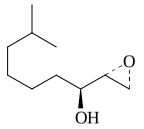
			**II**	NaOMe, MeOH	—	**I** (50)	159
			**I**	NaOD, D_2O, rt, 1 h	50:50	(—)[a]	24
C_8			**II**	KOH, H_2O, DMSO, 130–140°, 15 min	—	**I** (78)	183
			**II**	K_2CO_3, MeOH, rt, 24 h	—	**I** (71)	177
			**II**	K_2CO_3, MeOH, rt, 24 h	—	**I** (74)	177
			**II**	NaOH, H_2O	>90:10	(—)	205
			**I**	NaOH, H_2O	98:2	(—)	205

TABLE 1-A. EPOXIDE MIGRATION IN ACYCLIC SYSTEMS (*Continued*)

Major Isomer (**I**)	Minor Isomer (**II**)	Initial Isomer	Conditions	Final Mixture **I**:**II**	Final Mixture Yield (%)	Refs.
		**I**	$NaOH, H_2O$	92:8	(—)	205
		**II**	$NaOH, H_2O$, rt, 1 h	94:6[b]	(64)	206
		**I**	Na_2SO_3, MeOH, H_2O, rt, 12 h	60:40	(—)	178
C_{10} 		**II**	$NaOH, H_2O$, rt, 6 h	95:5	**I** (93)	207
		**I**	NaOMe, MeOH, reflux, 4 h	70:30	(—)	92
		**II**	K_2CO_3, MeOH, rt, 24 h	—	**I** (79)	177

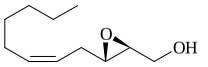
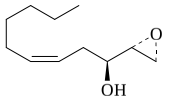
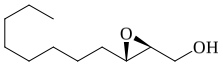
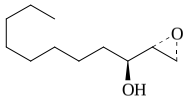
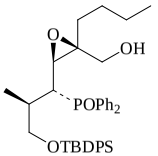
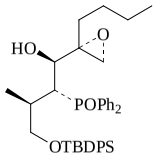
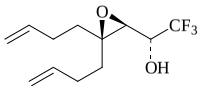
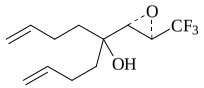
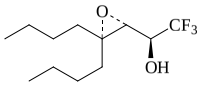
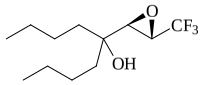
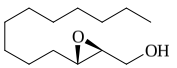
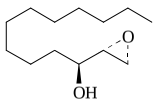
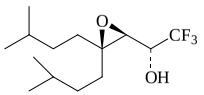
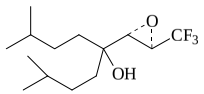
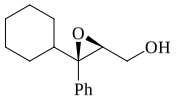
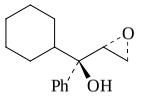
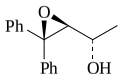
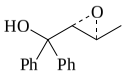
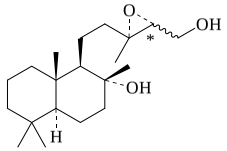
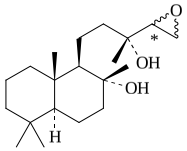
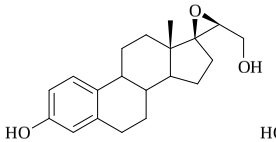
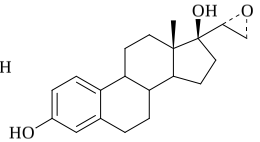
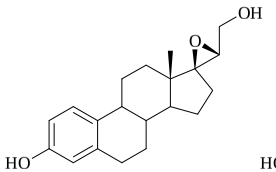
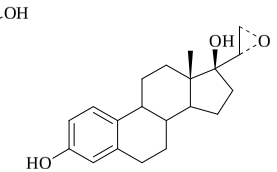
C_{11}			**II**	K_2CO_3, MeOH, rt, 24 h	—	**I** (73)	177
			**II**	K_2CO_3, MeOH, rt, 24 h	—	**I** (74)	177
			**II**	PhSLi, THF	—	**I** (42)[a,c]	208
C_{12}			**II**	NaOH, *t*-BuOH, H_2O, rt, 2 h	>300:1	(81)	73
			**II**	NaOH, acetone, H_2O, rt, 1 h	>300:1	(87)	73
C_{13}			**II** **II**	K_2CO_3, MeOH, rt, 24 h LiC_2Me, BF_3•Et_2O, THF, –70°, 3 h	— —	**I** (73) **I** (72)	177 209
C_{14}			**II**	NaOH, *t*-BuOH, H_2O, rt, 6 h	>155:1	(86)	73

TABLE 1-A. EPOXIDE MIGRATION IN ACYCLIC SYSTEMS (*Continued*)

	Major Isomer (**I**)	Minor Isomer (**II**)	Initial Isomer	Conditions	Final Mixture **I**:**II**	Final Mixture Yield (%)	Refs.
C_{15}			**II**	*t*-BuOK, DMF, rt, 1 h	—	**I** (85)	185
C_{16}			**II**	KOH, MeOH, H_2O, rt, 3 h	—	**I** (82)[a]	179
C_{19}			**II**	NaOH, H_2O, *t*-BuOH	—	**I** (91)[d]	210
C_{20}			**II**	K_2CO_3, MeOH, rt	—	**I** (80)	181
			**II**	*t*-BuOK, *t*-BuOH, 30–40°	—	**I** (89)[a]	181

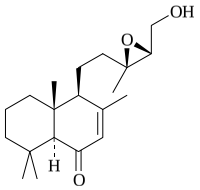
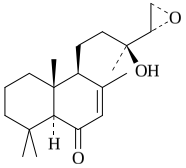
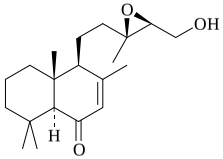
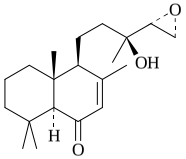
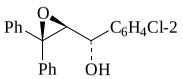
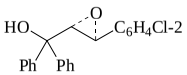
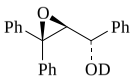
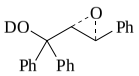
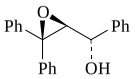
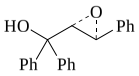
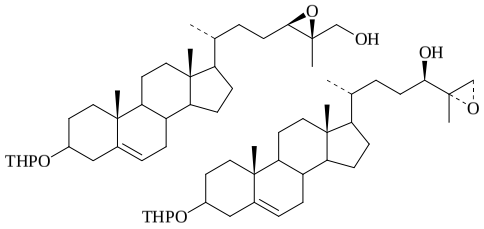
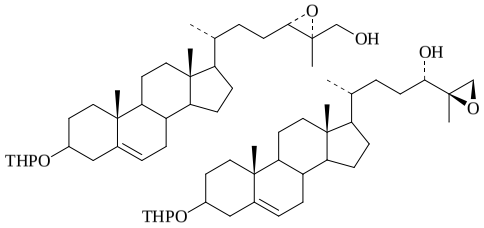
			**II**	$NaOH$, H_2O, *t*-BuOH, rt, 3 h	—	**I** (95)	130
			**II**	$NaOH$, H_2O, *t*-BuOH, rt, 3 h	—	**I** (95)	130
C_{21}			**II**	KOH, MeOH, rt, 15 h	—	**I** (95)	1
			**II**	$NaOCD_3$, CD_3OD	95:5	**I** (—)	70
			**II**	KOH, H_2O, MeOH, rt, 2 days	—	**I** (>60)	211

TABLE 1-A. EPOXIDE MIGRATION IN ACYCLIC SYSTEMS (*Continued*)

Major Isomer (**I**)	Minor Isomer (**II**)	Initial Isomer	Conditions	Final Mixture **I**:**II**	Final Mixture Yield (%)	Refs.
C_{27} 		**II**	K_2CO_3, *i*-PrOH, reflux, 2 h	—	**I** (84)	182
		**II**	K_2CO_3, *i*-PrOH, reflux, 2 h	—	**I** (85)	182

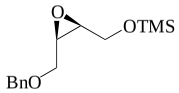
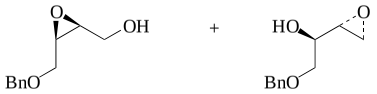
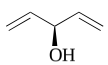
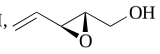
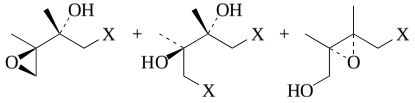
[a] See also Table VII under the same carbon count.

[b] The isomer ratio is based on isolated yield.

[c] The product was accompanied by the opening of **I** by PhS^- (**II**: RSPh = 42:58).

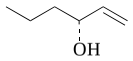
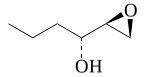
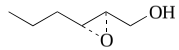
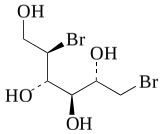
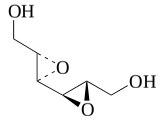
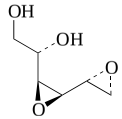
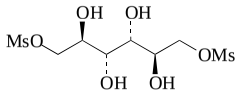
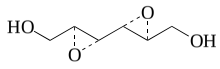
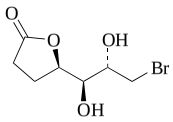
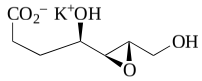
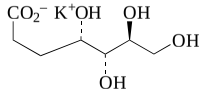
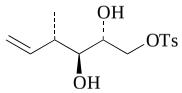
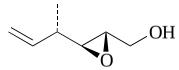
[d] Both isomers were 1:1 mixtures of stereoisomers at the position marked with an asterisk.

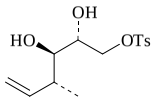
TABLE 1-B. EPOXY ALCOHOL FORMATION IN SITU AND EPOXIDE MIGRATION IN ACYCLIC SYSTEMS

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_4 	Bu_4NF, CH_2Cl_2, 25°, 20 h	 **I** + **II**[a] **I**:**II** = 2:1	25
C_5 	1. $Ti(OPr\text{-}i)_4$ (1 eq), *t*-BuO_2H, L-(+)-DET, CH_2Cl_2, –20° 2. tartaric acid, NaOH, H_2O	 (—)[b]	106
C_6 		 **I** **II** **III**[a]	212

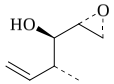
	X	**I** (%)	**II** (%)	**III** (%)
NaOMe, MeOH, rt, 24 h	OMe	52	14	31
PhSH, H_2O, 0°, 1.5 h	SPh	17	20	—
t-BuSH, H_2O, 0°, 0.3 h	SBu-*t*	67	24	—
1. NaN_3, acetone, H_2O, –22°, 10 h 2. rt, 10 h	N_3	16	1	26
Et_2NH, H_2O, 45°, 17 h	NEt_2	—	—	37
1. morpholine, THF, rt, 24 h 2. 60°, 48 h		—	7	10

TABLE 1-B. EPOXY ALCOHOL FORMATION IN SITU AND EPOXIDE MIGRATION IN ACYCLIC SYSTEMS (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
	Ti(OPr-*i*)$_4$ (100 mol%), *t*-BuO$_2$H, L-(–)-DET, CH_2Cl_2, –20°	 **I** +  **II**[a] **I**:**II** = 50:50 (—)[b]	213
	KOH, H_2O, 20°, 10 min	 (62)[a,b] +  (38)[a,b]	45
	1. NaOH, H_2O, pH > 12.6 2. Na_2CO_3, EtOAc	 (24)	214
C$_7$ 		 **I**[a,b] +  **II**[a,b]	32
		I:**II** KOH, H_2O, rt, 5 min — 100:0 KOH, H_2O, rt, 15 min — 2:1 KOH, H_2O, rt, 18 h — 0:100	
	NaOMe, MeOH, CH_2Cl_2, 22°, 15 min	 (80)[b]	200

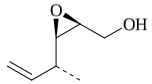


NaOMe, MeOH, CH_2Cl_2, 22^o, 15 min



I

+



II[a]

I:**II** = 50:50 (74)[b]

200

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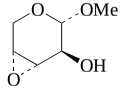
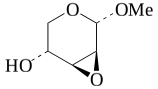
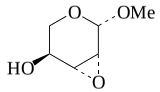
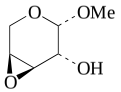
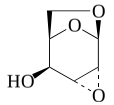
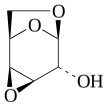
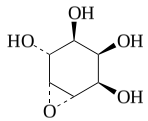
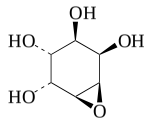
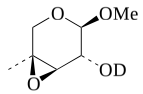
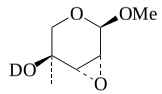
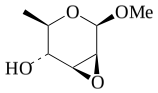
[a] This was the product of epoxide migration.

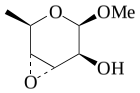
[b] See also Table VII under the same carbon count.

TABLE 2-A. EPOXIDE MIGRATION IN CYCLIC SYSTEMS

	Major Isomer (**I**)	Minor Isomer (**II**)	Initial Isomer	Conditions	Final Mixture **I**:**II**	Yield (%)	Refs.
C_5			**I**	$Ba(OH)_2$, H_2O, rt, 5 h	73:27[a]	(71)	77
			II	"	75:25[a]	(84)	77, 176
	α-D-arabino	α-D-lyxo					
			**I**	$Ba(OH)_2$, H_2O, rt, 5 h	67:33[a]	(82)	77
			II	"	70:30[a]	(83)	77
	β-L-lyxo	β-L-arabino					
C_6			**I**	NaOH, EtOH, H_2O	—	(—)	215
			II	NaOH, MeOH	80:20	(—)	80
	β-D-gulo	β-D-galacto					
			**II**	$Ba(OH)_2$, H_2O, rt, 5 h	90:10	(—)	2
			**II**	$NaOCD_3$, CD_3OD, rt, 2 h	90:10	(—)	70, 79
	α-L-arabino	α-L-lyxo					

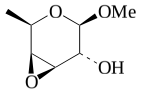


β-D-manno

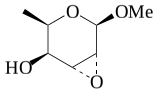


β-D-altro

I or **II**	NaOMe, MeOH, rt 16–20 h	67:33	(—)	75
II	NaOMe, MeOH, reflux, 1 h	—	**I** (79)	74

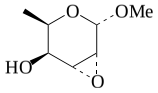


β-D-galacto

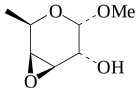


β-D-gulo

I or **II**	NaOMe, MeOH, rt, 15 h	—	**I** (70)	75
I or **II**	NaOMe, MeOH, rt, 16–20 h	90:10	(—)	

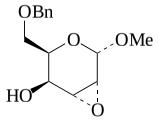


α-D-gulo

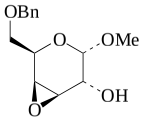


α-D-galacto

II	0.01 M NaOH, H_2O, 42°, 2.5 h	—	**I** (13)[b]	216
II	0.01 M NaOH, H_2O, 42°, 1.5 h	55:45		76

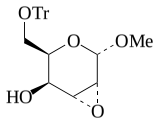


α-D-gulo

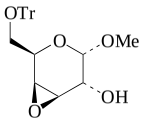


α-D-galacto

II	NaOMe, MeOH, rt, 1 h	55:45[a]	(83)	176, 217



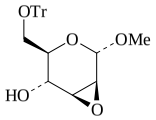
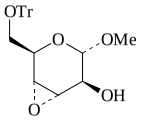
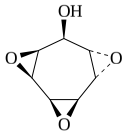
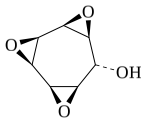
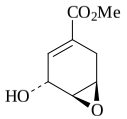
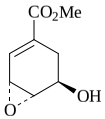
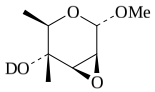
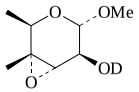
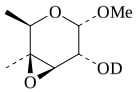
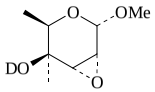
α-D-gulo



α-D-galacto

II	NaOMe, MeOH, rt, 1 h	55:45[a]	(78)	217

TABLE 2-A. EPOXIDE MIGRATION IN CYCLIC SYSTEMS (*Continued*)

Major Isomer (**I**)	Minor Isomer (**II**)	Initial Isomer	Conditions	Final Mixture **I**:**II**	Final Mixture Yield (%)	Refs.
 α-D-manno	 α-D-altro	**I**	NaOMe, MeOH, rt 1.5 h	—	**I** (85)	74
C_7 		**I**	LiOEt, EtOH, 60°, 7 h	—	(—)[c]	218
		**II**	"natural product isolation"	50:50	(—)	143, 144
		II	NaOMe, MeOH, rt	50:50	(—)[d]	219
		II	NaOMe, MeOH, rt	70:30	(—)	143, 144
		II	NaOMe, MeOH, 50°, 25 min	75:25	(—)	143, 144
 α-D-manno	 α-D-altro	**I**	$NaOCD_3$, CD_3OD, rt, 2 h	57:43	(—)	70, 79
 α-D-galacto	 α-D-gulo	**II**	$NaOCD_3$, CD_3OD, rt, 4 h	92:8	(—)	70, 79

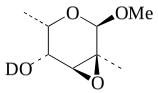
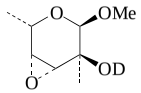
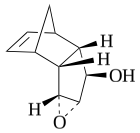
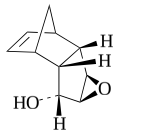
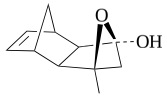
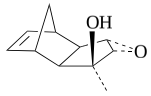
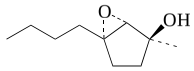
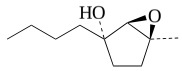
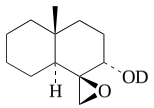
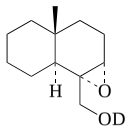
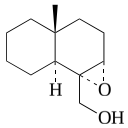
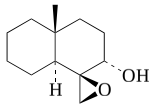
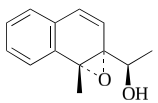
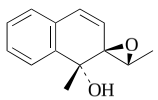
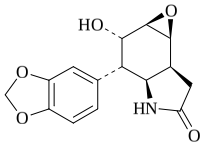
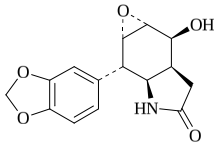
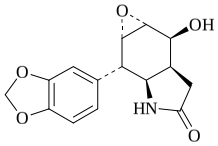
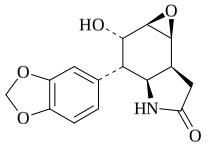
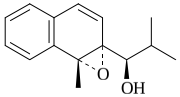
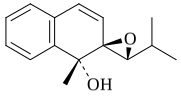
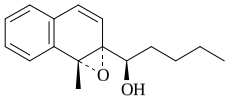
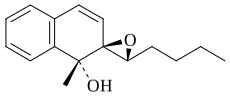
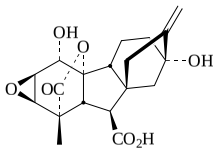
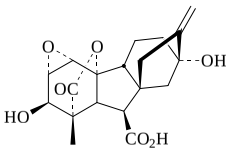
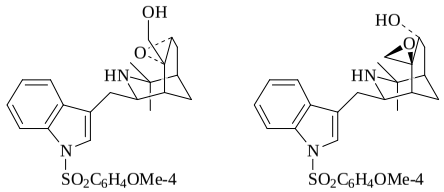
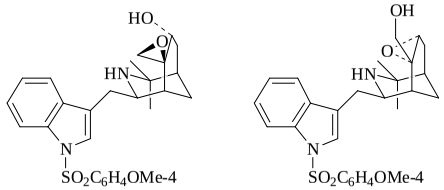
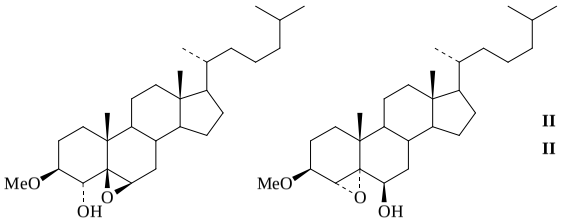
	 α-L-gulo	 α-L-galacto	**I** or **II**	$NaOCD_3$, CD_3OD, rt, 2 h	93:7	(—)	70, 79
C_{10}			**I** or **II**	LDA	100:0	(—)	84
			**I** or **II**	LDA	100:0	(—)	84
			**II**	BuLi, THF, −78° to rt, 1h	80:20	(90)	186
C_{12}			**II**	NaOD, DMSO-d_6, rt, 2 h	2:1	(—)	220
			**I**	NaOH, H_2O, rt, 5 h	2:1	(—)	220
C_{13}			**II**	LiOH, H_2O, Et_2O, 23°, 4 h	—	**I** (90)	180

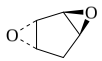
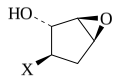
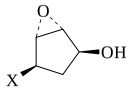
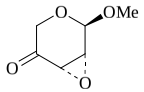
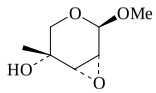
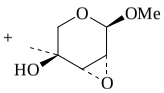
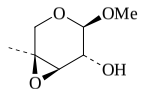
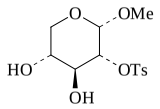
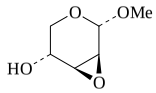
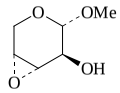
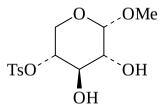
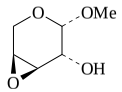
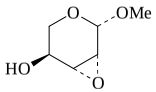
TABLE 2-A. EPOXIDE MIGRATION IN CYCLIC SYSTEMS (*Continued*)

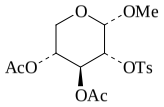
	Major Isomer (**I**)	Minor Isomer (**II**)	Initial Isomer	Conditions	Final Mixture **I**:**II**	Yield (%)	Refs.
C_{14}			**II**	NaH, THF, 40°, 9.5 h	86:14[a]	(71)	184
			II	CaH_2, THF, 50°, 5 h	90:10[a]	(65)	
			**II**	KH, THF, 40°, 6.5 h	69:31[a]	(100)	184
C_{15}			**II**	LiOH, H_2O, Et_2O, 23°, 4 h	—	**I** (73)	180
C_{16}			**II**	LiOH, H_2O, Et_2O, 23°, 4 h	—	**I** (82)	180
C_{18}			**I**	KOH, H_2O	74:26[a]	(92)	140

C_{20}		**II**	$LiBHEt_3$, THF, 25°, 16 h	—	**I** (80)	82
		**II**	$NaBH_4$, NaOH, *t*-BuOH, 25°, 12 h	—	**I** (85)	82
C_{27}		**II**	KOH, MeOH, reflux, 1.5 h	—	(68)	50, 52
		II	"	—	(76)	50, 52

[a] The isomer ratio is based on isolated yield.
[b] The product was isolated as the acetate.
[c] Additional products due to decomposition were identified.
[d] See also Table VII under the same carbon count.

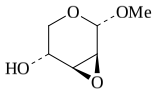
TABLE 2-B. EPOXY ALCOHOL FORMATION IN SITU AND EPOXIDE MIGRATION IN CYCLIC SYSTEMS

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_5 		 +  **I** **II**[a]	221
		X: **I** (%): —[b]; **II** (%): 12[b]	
	Me_2NH, H_2O, 25°, 15 h	Me_2N	
	piperidine, 90°, 0.5 h	 34; 20	
	morpholine, 25°, 13 h	 —; 46	
	1. MeLi, THF, Et_2O, –78° 2. H_2O, HOAc, –25°	 +  +  β-D-ribo (35) α-L-lyxo (22) α-L-arabino (19)[a]	70
 α-D-xylo	NaOMe, MeOH, 55-60°, 1 h	 +  α-D-lyxo (67) α-D-arabino (15)[a]	77
 α-D-xylo	NaOMe, MeOH, rt, 1.5 h	 +  β-L-arabino (87) β-L-lyxo (—)[a]	77

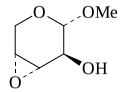


α-D-xylo

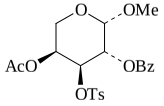
NaOMe, MeOH, rt, overnight



α-D-lyxo (75) +

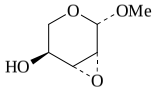


α-D-arabino (16)[a] 176

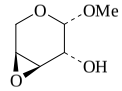


β-L-arabino

NaOMe, MeOH, rt, 6 h



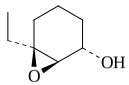
β-L-lyxo (52) +



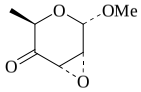
β-L-arabino (9)[a] 77

C_6

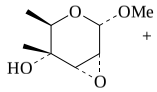
1. EtMgBr, THF, –70 to –15°, 12 d
2. NH_4Cl, H_2O



(37)[b] 222



1. MeLi, THF, Et_2O, –78°



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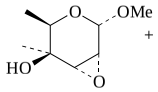

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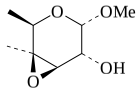
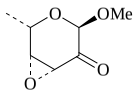
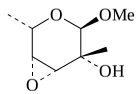


α-D-allo (**I**)[b] α-D-gulo (**II**)[b] α-D-galacto (**III**)[a] 70

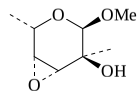
	I (%)	**II** (%)	**III** (%)
2. HOAc, –78°	42	47	6
2. HOAc, –25°	37	34	26
2. H_2O, 0°	49	6	40



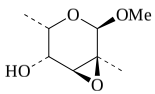
1. MeLi, THF, Et_2O, –78°
2. H_2O, HOAc, –25°



+

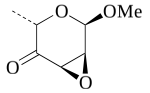
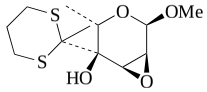
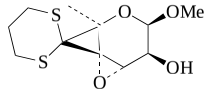
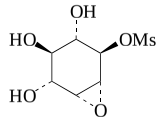
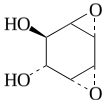
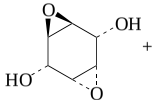
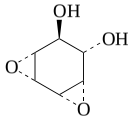
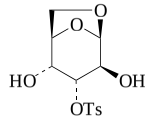
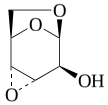
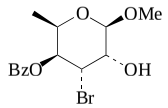
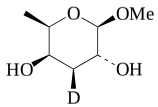
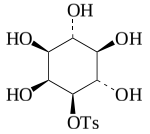
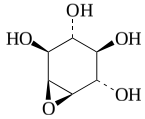


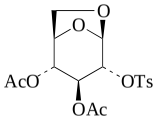
+



α-L-talo (38) α-L-galacto (22) α-L-gulo (20)[a] 70

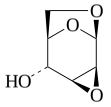
TABLE 2-B. EPOXY ALCOHOL FORMATION IN SITU AND EPOXIDE MIGRATION IN CYCLIC SYSTEMS (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
	 , BuLi, THF	 (26) +  $(7)^a$	223
	$NaOMe, CHCl_3, MeOH$	 (0) +  $(60)^a$ +  $(0)^a$	224
 β-D-altro	NaOMe, MeOH, reflux, 4 h NaOH, H_2O, rt, 24 h	 β-D-altro (20) (85)	78, 81 78, 81
 β-D-gulo	1. NaOMe, CH_2Cl_2 2. $LiAlD_4$, THF	 (75)	225
	$Ba(OH)_2$, H_2O, rt, 5 h	 $(6)^b$	226



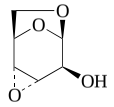
β-D-gluco

NaOMe, MeOH, rt, 12 h



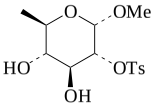
β-D-manno (—)

+



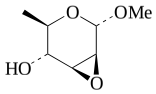
β-D-altro (85)[a]

227



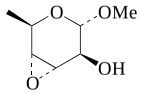
α-D-gluco

NaOMe, MeOH,
reflux, 90 min



α-D-manno (**I**)

+

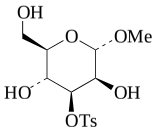


α-D-altro (**II**)[a]

(68–72)

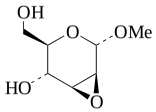
228

I:**II** <1:9



α-D-manno

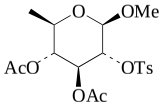
NaOH, H_2O, rt, 18 h



α-D-manno

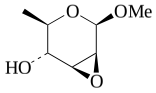
(46)[b]

74



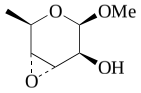
β-D-gluco

NaOMe, MeOH, rt, 16 h



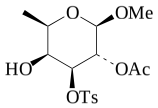
β-D-manno (40)

+



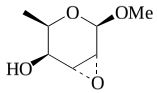
β-D-altro (21)[a]

75



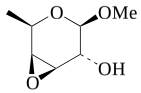
β-D-galacto

NaOMe, MeOH, rt, 6 h



β-D-gulo
(initially)

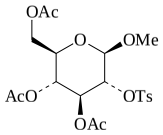
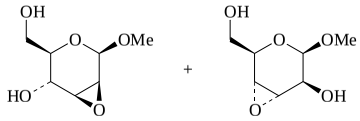
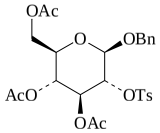
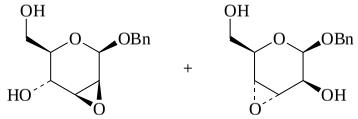
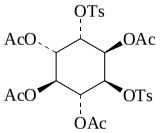
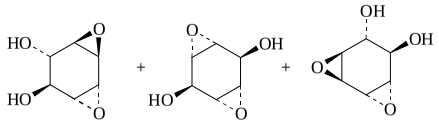
+

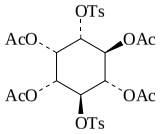


β-D-galacto
(strongly preferred)[a]

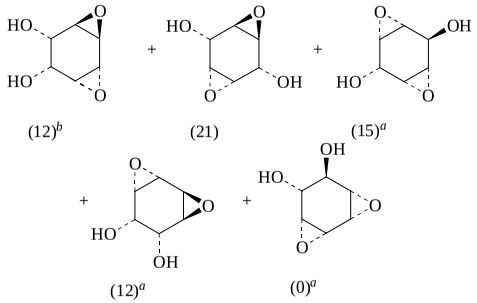
75

TABLE 2-B. EPOXY ALCOHOL FORMATION IN SITU AND EPOXIDE MIGRATION IN CYCLIC SYSTEMS (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
 β-D-gluco	NaOMe, MeOH	 β-D-manno (major) + β-D-altro (minor)[a]	229
 β-D-gluco	NaOMe, MeOH, rt, 6 h	 β-D-manno (65) + β-D-altro (29)[a]	230
	NaOMe, MeOH, $CHCl_3$	 (10)[b] + (15)[a] + (10)[a]	224

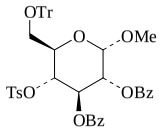


NaOMe, MeOH, $CHCl_3$



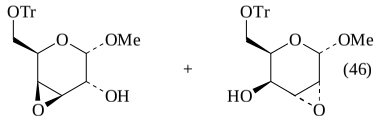
(12)[b] (21) (15)[a] (12)[a] (0)[a]

224



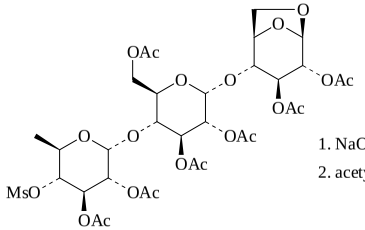
α-D-gluco

NaOH, H_2O, reflux, 1.5 h

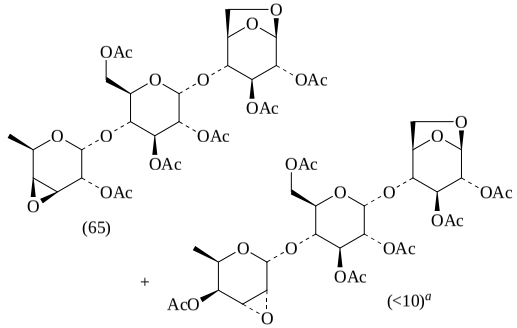


α-D-gulo (—)[b] (46) α-D-galacto (—)[a]

231, 232



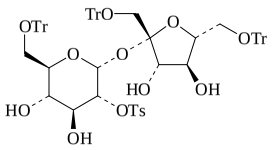
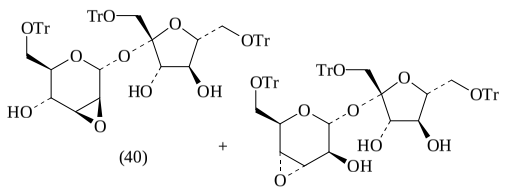
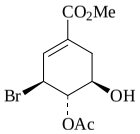
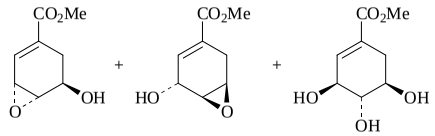
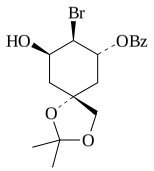
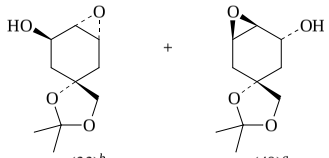
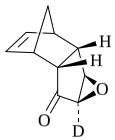
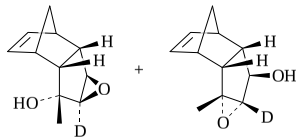
1. NaOMe, CH_2Cl_2, MeOH, 50°
2. acetylation

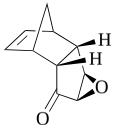


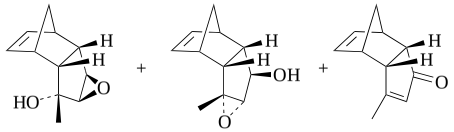
(65) (<10)[a]

233

TABLE 2-B. EPOXY ALCOHOL FORMATION IN SITU AND EPOXIDE MIGRATION IN CYCLIC SYSTEMS (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
	1. NaOMe, MeOH, reflux, 2 h	 (40) + (15)[a]	96
C_7 	1. NaOMe, MeOH, 0°, 30 min 2. 50°, 35 min	 (15)[b] + (46)[a] + (28)[a]	143, 144
	NaOMe, MeOH, THF, reflux	 (33)[b] + (48)[a]	234
C_{10} 	MeMgI, THF, Et_2O, rt, 3 d	 (11) + (70)[a]	84



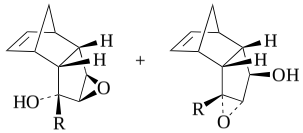


I II^a III^a

84

	I:II:III
MeLi, LiCl, THF, rt, 4 d	57:43:0
MeLi, THF, rt, 4 d	47:53:0
MeLi, ether, rt 10 d	49:35:16
MeMgI, THF, rt, 3 d	0:100:0

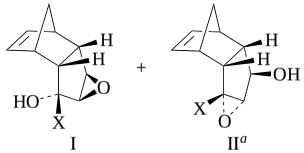
RLi, THF, 0^o



I II^a

R	**I** (%)	**II** (%)
Me	77	15
Bu	—	—

104



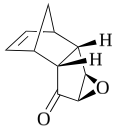
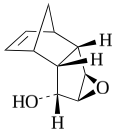
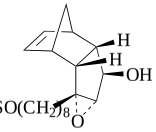
I II^a

84, 235

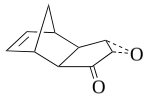
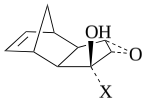
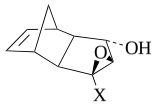
X	**I:II**
H	84:16
Me	86:14
n-Bu	70:30
s-Bu	24:76
t-Bu	0:100

$NaBH_4$, THF, rt, 3 d
MeLi, THF, rt, 1 h
n-BuLi, THF, rt, 1 h
s-BuLi, THF, rt, 1 h
t-BuLi, THF, rt, 1 h

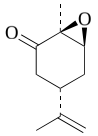
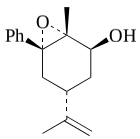
TABLE 2-B. EPOXY ALCOHOL FORMATION IN SITU AND EPOXIDE MIGRATION IN CYCLIC SYSTEMS (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
	$M(CH_2)_8OTBDMS$, THF	 +  I / II[a]	236

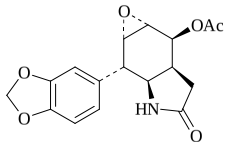
M	**I** (%)	**II** (%)
BrMg	40	24
Li	0	89

		 +  I / II[a]		84

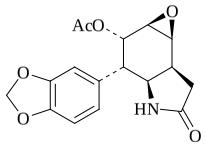
X	**I:II**
H	71:29
H	65:28
Me	100:0
n-Bu	0:100
s-Bu	0:100
t-Bu	0:100
Ph	74:26

	PhMgBr, THF		(51)	237

C_{14}

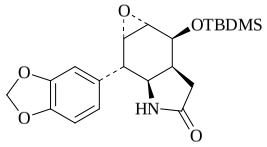


1. 5% K_2CO_3, MeOH, rt, 3 h
2. Ac_2O, py

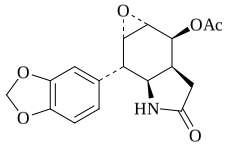


(61)

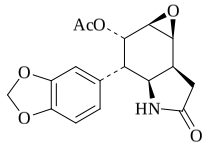
184



1. Bu_4NF, THF
2. Ac_2O, py



+



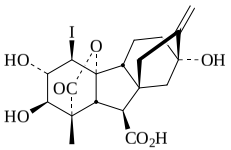
184

I

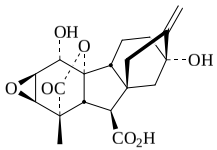
II^a

	I (%)	**II** (%)
rt, 0.5 h	77	11
rt, 20 h	35	25
40°, 8 h	30	26

C_{18}



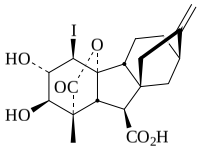
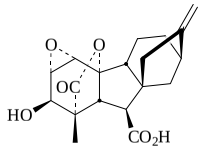
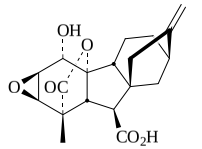
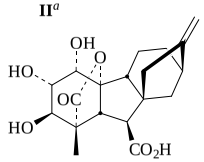
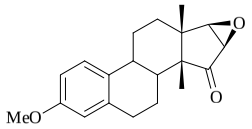
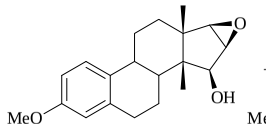
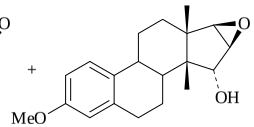
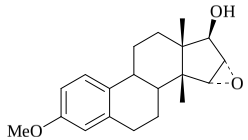
KOH, H_2O, rt, 6 h

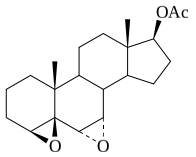


(63)

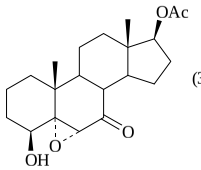
140

TABLE 2-B. EPOXY ALCOHOL FORMATION IN SITU AND EPOXIDE MIGRATION IN CYCLIC SYSTEMS (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
	K_2CO_3, MeOH, rt, 4 h KOH, H_2O, rt 2 h	 +  +  I **II**[a] **III**[a] **I** (%) **II** (%) **III** (%) 16 75 — — 80 5	140
C_{19} 	$LiAlH_4$, THF, 0^o to rt, 1.5 h	 +  (86) (1) +  (8)[a]	238



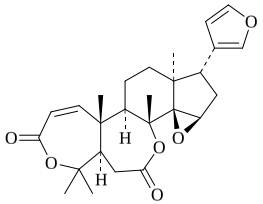
$KMnO_4$, $CuSO_4$



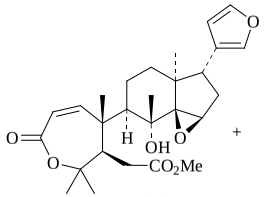
(39)

239

C_{26}

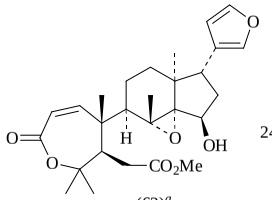


KOH, MeOH, H_2O, rt, 70 min



(31)

+



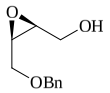
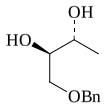
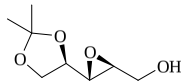
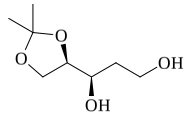
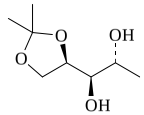
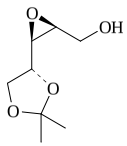
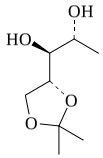
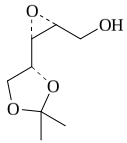
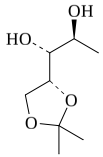
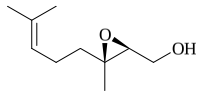
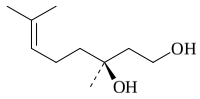
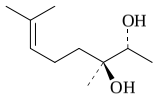
(62)[a]

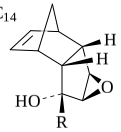
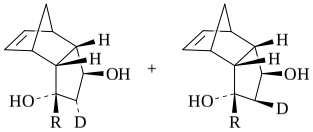
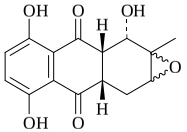
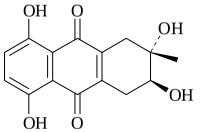
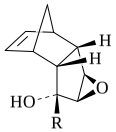
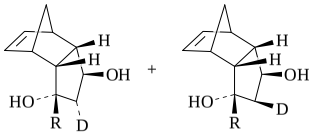
240

[a] This was a product of epoxide migration.

[b] See also Table VII under the same carbon count.

TABLE 3-A. EPOXIDE MIGRATION WITH REDUCTION IN SITU

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_4 	$NaBH_4$, NaOH, H_2O, *t*-BuOH, reflux	 (70)	4
C_5 	$NaBH_4$, NaOH, H_2O, *t*-BuOH, reflux	 (15) +  (39)[a]	4
	$NaBH_4$, NaOH, H_2O, *t*-BuOH, reflux	 (60)	4
	$NaBH_4$, NaOH, H_2O, *t*-BuOH, reflux	 (67)	4
C_{10} 	$NaBH_4$, NaOH, H_2O, *t*-BuOH, reflux	 (24) +  (53)[a]	4

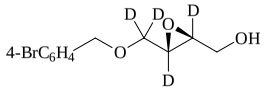
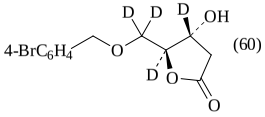
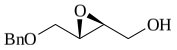
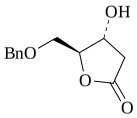
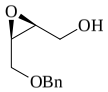
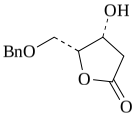
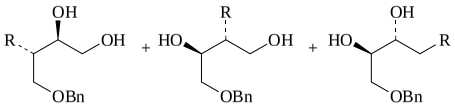
C_{11}–C_{14} 	$LiAlD_4$, THF, rt, 1 d	 I + **II**[a]		84
	$LiAlD_4$, THF, rt, 4–6 d			104
	$LiAlD_4$, THF, rt, 4–6 d			104
C_{15} 	NaOMe, MeOH		(23)	241
C_{18} 	$LiAlD_4$, THF, rt, 1 d	 I + **II**[a]		104

R	**I:II**	(%)
Me	0:100	48
Me	63:37	92
n-Bu	51:49	90

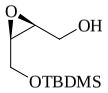
R	**I:II**	(%)
n-C_8H_{17}	53:47	87
$CH_2(CH_2)_7OTBDMS$	45:55	77
$CH_2C{\equiv}CC_5H_{15}$-*n*	65:35	81

[a] This was a product of epoxide migration.

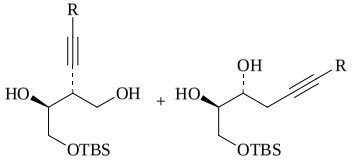
TABLE 3-B. EPOXIDE MIGRATION WITH *C*-NUCLEOPHILE OPENING IN SITU

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_4 	1. NaCN, EtOD, D_2O, reflux, 8 h 2. HCl 3. toluene, reflux	 (60)	85
	1. NaCN, MeOH, H_2O, dioxane, 80° 2. H^+	 (35)	4
	1. NaCN, EtOH, H_2O, reflux, 8 h 2. toluene, azeotrope	 (38)	187
	RM, LiCl, THF, 0 to 25°	 **I** **II** **III**[a]	25, 90

R	RM	**I**:**II**:**III**	(%)
Me	MeCu	1:1:50	94
Me	MeCuCNLi	1:1:50	95
Me	Me_2CuLi	2:3:1	95
Bu	BuCuCNLi	1:1:50	90
Ph	PhCu•DMS	1:1:50	92
$CH_2=C(CH_3)$	$[CH_2=C(CH_3)]_2CuCNLi_2$	1:1:20	86



RC≡CLi, BF_3•Et_2O, –70°, 1 h

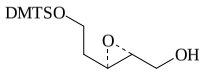


87

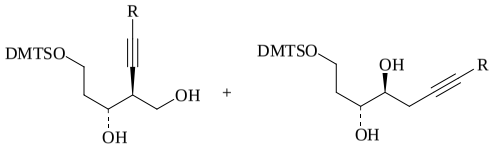
I **II**[a]

R	**I** (%)	**II** (%)
n-C_5H_{11}	40	40
n-C_8H_{17}	32	51
n-$C_{11}H_{23}$	19	59

C_5



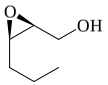
RC≡CLi, BF_3•Et_2O, –70°, 1 h



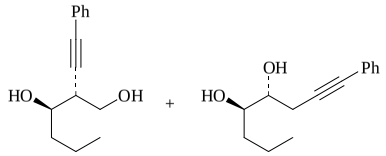
88

R = *n*-C_9H_{19} (17) (75)[a]

C_6



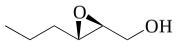
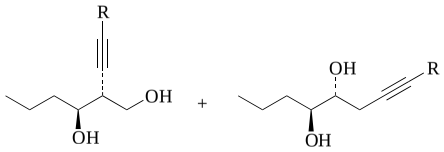
PhC≡CLi, BF_3•Et_2O, –78°, 30 min



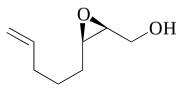
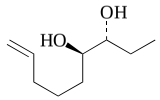
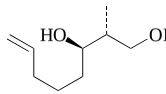
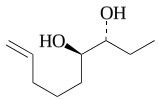
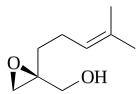
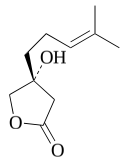
89

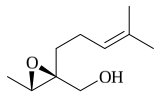
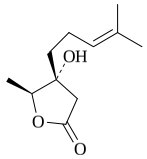
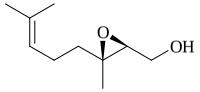
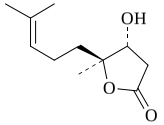
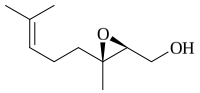
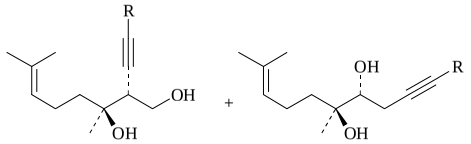
(47) (34)[a]

TABLE 3-B. EPOXIDE MIGRATION WITH *C*-NUCLEOPHILE OPENING IN SITU(*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
	$RC{\equiv}CLi$, $BF_3{\bullet}Et_2O$, –78°, 30 min	 **I** + **II**[a]	89

R	**I**:**II**	**II** (%)
n-C_5H_{11}	19:81	81
Ph	28:72	77

C_8 	1. BuLi, LiCl, THF, –78° 2. MeCu(CN)Li, 0°, 5 min 3. rt, 16 h	 (60)		25, 90
	1. BuLi, LiCl, THF, –78° 2. $(MeLi)_{1.2}CuCN$, 0°, 30 min 3. rt, 4 days	 (29) +  (62)[a]		25
C_9 	1. NaCN, EtOH, H_2O, reflux, 16 h 2. toluene, azeotrope	 (65)		86

C_{10} 	1. NaCN, EtOH, H_2O, reflux, 16 h 2. toluene, azeotrope		(56)	86
	1. NaCN, EtOH, H_2O, reflux, 5.5 h 2. TsOH, benzene, reflux, 1 h		(40)	131
	RC≡CLi, BF_3•Et_2O, –78°, 30 min			89

I	**II**[a]

R	**I**:**II**	**II** (%)
n-C_5H_{11}	20:80	87
Ph	45:55	94

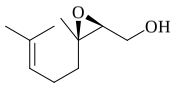
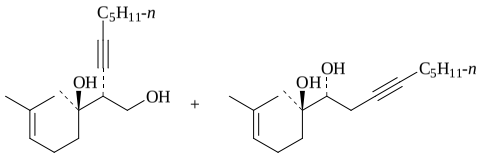
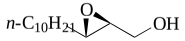
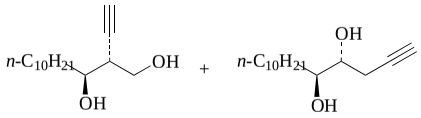
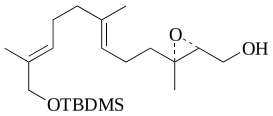
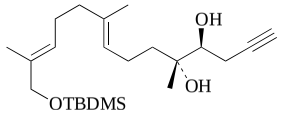
	*n*-$C_5H_{11}C{\equiv}CLi$, BF_3•Et_2O, –78°, 30 min		(50) (50)	89

TABLE 3-B. EPOXIDE MIGRATION WITH *C*-NUCLEOPHILE OPENING IN SITU (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{13} 	$HC{\equiv}CLi$, $BF_3{\bullet}Et_2O$, –78°	 (18) + (57)[a]	89
C_{15} 	C_2H_2, *n*-BuLi, $BF_3{\bullet}Et_2O$, THF, –78 to –40°	 (72)	242

[a] This was a product of epoxide migration.

TABLE 3-C. EPOXIDE MIGRATION WITH *N*-NUCLEOPHILE OPENING IN SITU

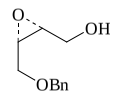
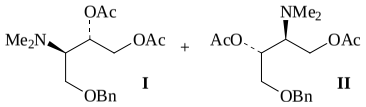
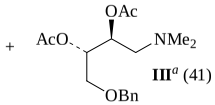
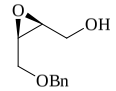
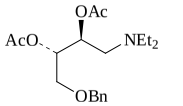
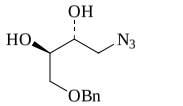
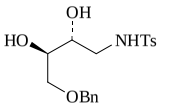
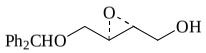
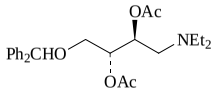
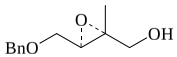
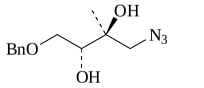
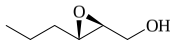
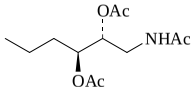
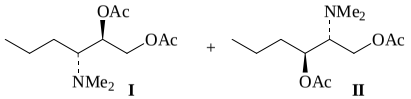
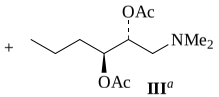
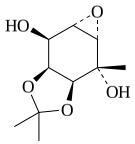
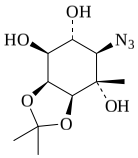
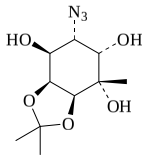
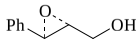
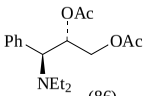
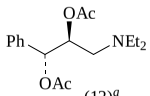
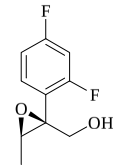
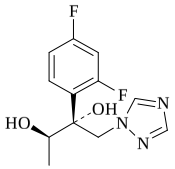
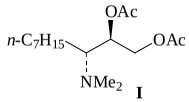
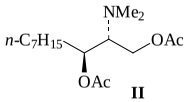
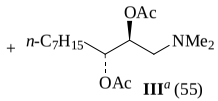
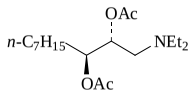
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_4 	1. Me_2NH, KOH, H_2O, rt 2. Ac_2O, py	 **I** + **II** +  **III**[a] (41) **I**:**II**:**III** = 4:21:75 (89)	91
	1. Et_2NH, KOH, H_2O, reflux 2. Ac_2O, py	 (45)[b]	91
	NaN_3, $LiClO_4$, MeCN	 (89)[c]	93
	NaNHTs, H_2O, dioxane, 60°	 (61)	4
	1. Et_2NH, KOH, H_2O, reflux 2. Ac_2O, py	 (64)[b]	91

TABLE 3-C. EPOXIDE MIGRATION WITH *N*-NUCLEOPHILE OPENING IN SITU (*Continued*)

	Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_5		NaN_3, *n*-$C_{16}H_{33}NMe_3Br$, 1,4-dioxane, H_2O, 100°	 (52)	94
C_6		1. NH_3, KOH, H_2O 2. Ac_2O, py	 (<30)	91
		1. Me_2NH, Me_4NOH, H_2O, rt 2. Ac_2O, py	 **I** + **II**	91
			+  **III**[a] **I:II:III** = 19:7:74 (94)	
C_7		NaN_3, DMF, H_2O, reflux, 14 h	 (30) +  (25)[a]	95
C_9		1. Et_2NH, KOH, H_2O, rt 2. Ac_2O, py	 (86) +  (12)[a]	91

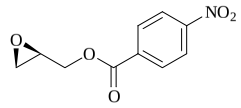
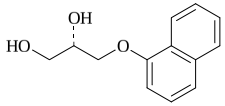
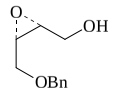
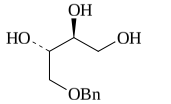
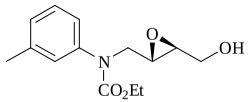
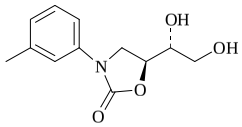
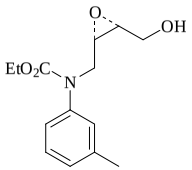
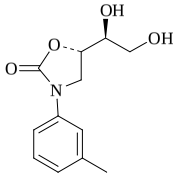
C_{10} 	1,2,4-triazole, *t*-BuOK, *t*-BuOH, 70°, 15 h		(59)	92
	1. Me_2NH, KOH, H_2O, rt 2. Ac_2O, py	 **I** +  **II** +  **III**[a] (55)	**I**:**II**:**III** = 20:7:73 (94)	91
	1. Et_2NH, KOH, H_2O, reflux 2. Ac_2O, py		(63)[b]	91

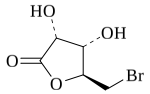
[a] This was a product of epoxide migration.

[b] This was the yield of purified product. Significant amounts of other isomers were present in the crude mixture.

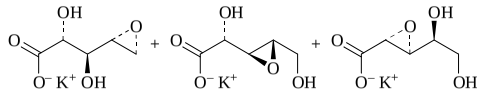
[c] See also Table VII under the same carbon count.

TABLE 3-D. EPOXIDE MIGRATION WITH *O*-NUCLEOPHILE OPENING IN SITU

	Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_3		1-Naphthol, NaOH, *t*-BuOH, H_2O	 (54)	38
C_4		NaOH, H_2O, *t*-BuOH, reflux	 (—)	243
		NaOH, H_2O, *t*-BuOH, 80°, 1 h	 (70–80)	244
		NaOH, H_2O, *t*-BuOH, 80°, 1 h	 (70–80)	244

C_5 

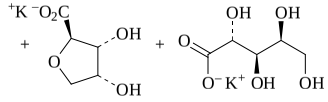
KOH, H_2O, rt



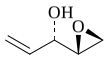
I **II**[a] **III**[a]

245

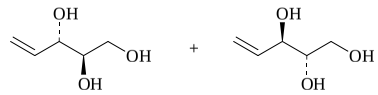
time	**I** (%)	**II** (%)	**III** (%)	**IV** (%)	**V** (%)
5 min	43	18	0	14	24
15 min	23	28	0	12	37
2 h	0	12	25	13	50
24 h	0	7	20	12	61
48 h	0	0	0	15	85



IV **V**

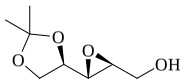


KOH, H_2O, dioxane, reflux, 16 h

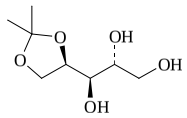


I **II**[a] **I**:**II** = 14:86

36, 37

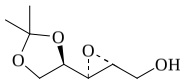


NaOH, H_2O, *t*-BuOH, 70°, 15 h

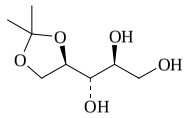


(79)

31

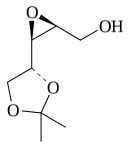


NaOH, H_2O, *t*-BuOH, 70°, 15 h

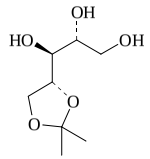


(75)

31



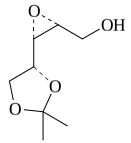
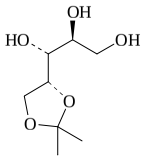
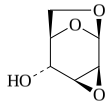
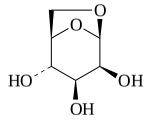
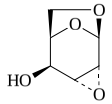
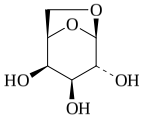
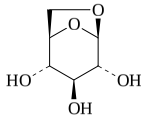
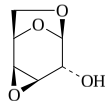
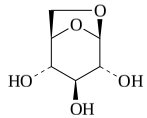
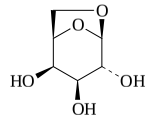
NaOH, H_2O, *t*-BuOH, 70°, 15 h



(75)

31

TABLE 3-D. EPOXIDE MIGRATION WITH *O*-NUCLEOPHILE OPENING IN SITU (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
	$NaOH, H_2O, t$-BuOH, 70°, 15 h	 (78)	31
C_6  β-D-manno	KOH, H_2O, 100°, 5 h	 β-D-manno (—)[b]	111
 β-D-gulo	KOH, H_2O, 100°, 5 h	 β-D-galacto (**I**) +  β-D-gluco (**II**)[a] **I**:**II** 83:17 (—)	111
 β-D-galacto	KOH, H_2O, 100°, 5 h	 β-D-gluco (**I**) +  β-D-galacto (**II**)[a] **I**:**II** 17:83 (—)	111

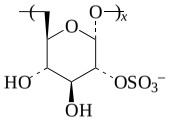
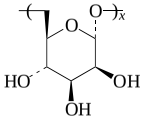
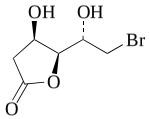
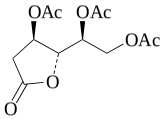
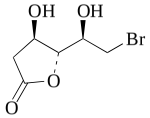
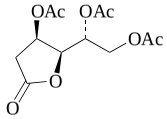
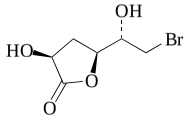
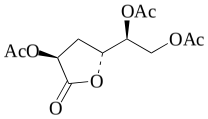
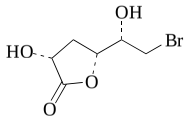
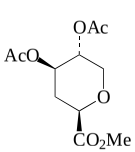
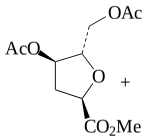
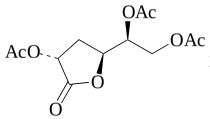
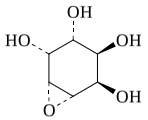
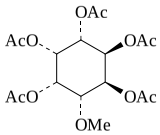
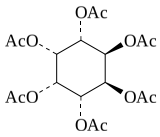
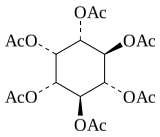
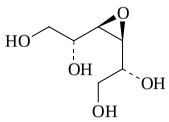
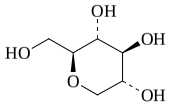
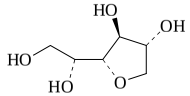
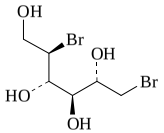
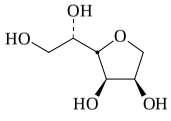
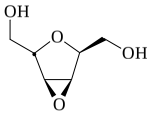
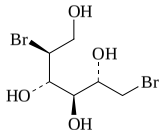
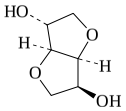
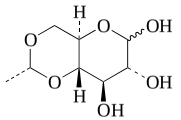
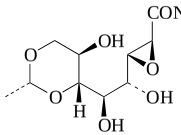
	 dextran sulfate	$NaOH, H_2O, 100^0, 5$ h	 α-D-manno	(—)	246, 247
C_6		1. KOH, H_2O, rt 2. Ac_2O, $HClO_4$		(48)	191
		1. KOH, H_2O, rt 2. Ac_2O, $HClO_4$		(44)	191
		1. KOH, H_2O, rt 2. Ac_2O, $HClO_4$		(56)	192
		1. KOH, H_2O, rt 2. H_2SO_4, MeOH 3. Ac_2O, py	 (30) +  (22) +  $(8)^a$		192

TABLE 3-D. EPOXIDE MIGRATION WITH *O*-NUCLEOPHILE OPENING IN SITU (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
	1. NaOMe, rt, 24 h 2. reflux, 5 h 3. Ac_2O, py	 (—)	2
	1. $Ba(OH)_2$, rt 2. 100°, 3 h 3. Ac_2O, py	 +  (21)[a] (9)[a]	2
	$NaOH, H_2O$, 100°, 1.5 h	 +  (27)[a] (53)[a]	54
	KOH, H_2O, 20°, 20 h	 +  (5)[c] (52)[a]	45
	KOH, H_2O, 20°, 30 min	 (74)	45

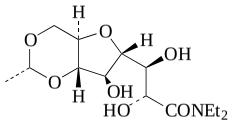


1. $Me_2\overset{+}{S}\overset{-}{C}HCONEt_2$, THF, 0°, 2 days
2. rt, 1 day



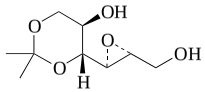
(70)[c]

+

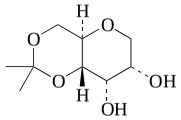


(16)[a]

248

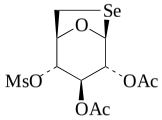


NaOH, *t*-BuOH, reflux, 24 h

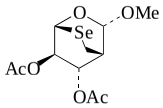


(80)

249

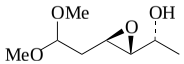


1. NaOMe, MeOH, rt, 48 h
2. Ac_2O, py

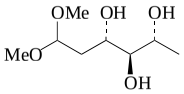


(23)

250

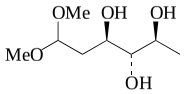


NaOH, H_2O, 80°, 6 h



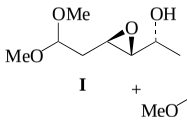
(20)

+



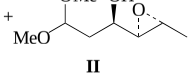
(68)[a]

35



I

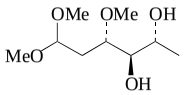
+



II

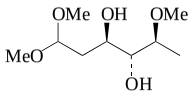
I:**II** = 57:43

NaOMe, MeOH, 70°, 15 h



III[a]

+



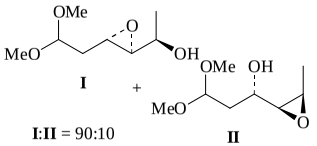
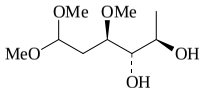
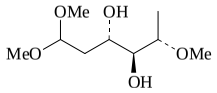
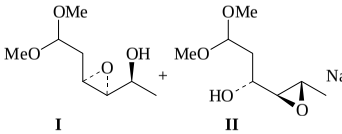
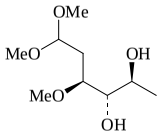
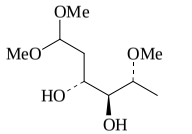
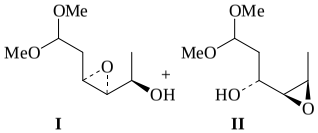
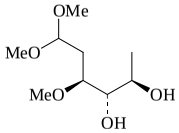
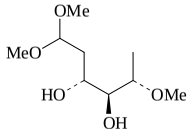
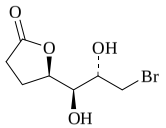
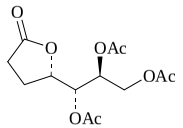
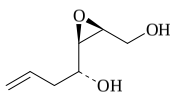
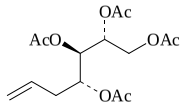
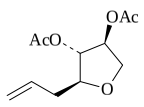
IV[a]

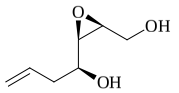
(—)

III:**IV** = 34:66

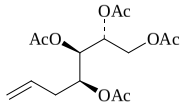
83

TABLE 3-D. EPOXIDE MIGRATION WITH *O*-NUCLEOPHILE OPENING IN SITU (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
 **I** + **II** **I:II** = 90:10	NaOMe, MeOH, 70°, 15 h	 **III**[a] +  **IV**[a] **III:IV** = 55:45	(—) 83
 **I** **I:II** = 7:93 **II**	NaOMe, MeOH, 70°, 15 h	 **III**[a] +  **IV**[a] **III:IV** = 18:82	(—) 83
 **I** **I:II** = 45:55 **II**	NaOMe, MeOH, 70°, 15 h	 **III**[a] +  **IV**[a] **III:IV** = 63:37	(80) 83
C_7 	1. KOH, H_2O, rt 2. Ac_2O, py	 (47)	32
	1. NaOH, H_2O, *t*-BuOH, reflux 2. Ac_2O, py	 (18)[a] +  (36)[a,b]	133

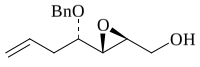


1. NaOH, H_2O, *t*-BuOH, reflux
2. Ac_2O, py

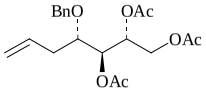


(45)

133

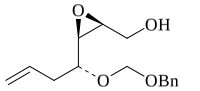


1. NaOH, H_2O, *t*-BuOH, 70°, 24 h
2. Ac_2O, Et_3N, DMAP

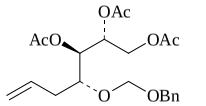


(65)

133

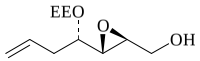


1. NaOH, H_2O, *t*-BuOH, 70°, 24 h
2. Ac_2O, Et_3N, DMAP

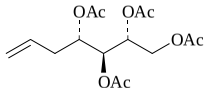


(60)

133



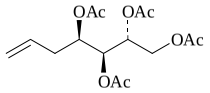
1. NaOH, H_2O, *t*-BuOH, reflux
2. HCl
3. Ac_2O, py



(66)

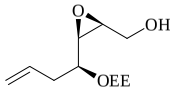
133

1. NaOH, H_2O, *t*-BuOH, reflux
2. HCl
3. Ac_2O, py

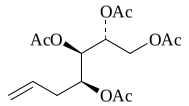


(66)

133



1. NaOH, H_2O, *t*-BuOH, reflux
2. HCl
3. Ac_2O, py



(73)

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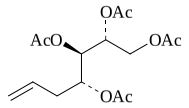
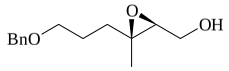
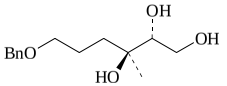
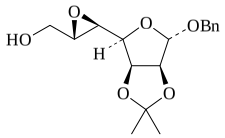
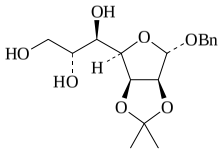
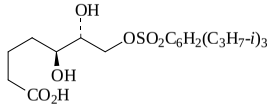
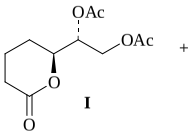
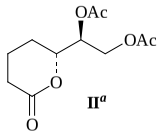
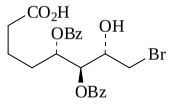
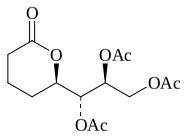
1. NaOH, H_2O, *t*-BuOH, reflux
2. HCl
3. Ac_2O, py

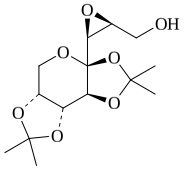


(97)

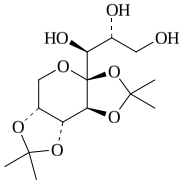
133

TABLE 3-D. EPOXIDE MIGRATION WITH *O*-NUCLEOPHILE OPENING IN SITU (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
	KOH, DMSO, H_2O, 12 h	 (50)	251
	NaOH, H_2O, 1,4-dioxane, 70^0, 40 h	 (63)	252
		 **I** +  **II**[a]	
	1. NaOH, EtOH, H_2O 2. acetylation	**I**:**II** = 16:84 (—)	34
	1. NaOEt, EtOH, rt, 18 h 2. OH^-, H_2O, EtOH, rt, 1 h 3. Ac_2O, py	**II** (88)	33, 34
C_8 	1. NaOEt, EtOH, rt, 24 h 2. OH^-, H_2O, EtOH, rt, 1 h 3. Ac_2O, py	 (68)	33

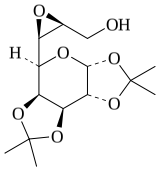


NaOH, H_2O, 1,4-dioxane, 70°, 24 h

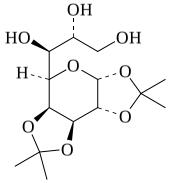


(37)

253

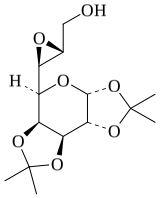


NaOH, H_2O, 1,4-dioxane, 70°, 24 h

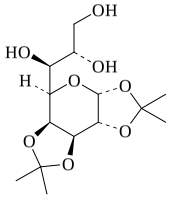


(64)

254, 255

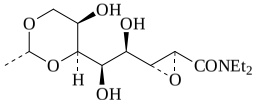


NaOH, H_2O, 1,4-dioxane, 70°, 18 h

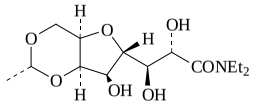


(52)

254

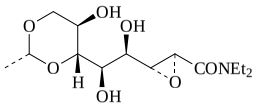


KOH (0.1%), MeOH, rt, 30 days

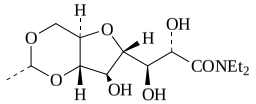


(54)

248



KOH (0.1%), MeOH, rt, 30 days



(12)

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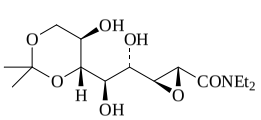
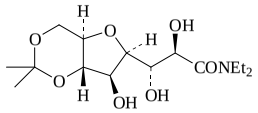
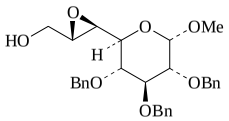
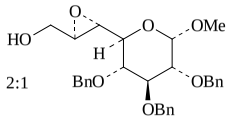
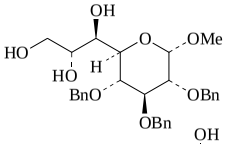
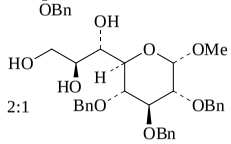
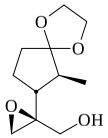
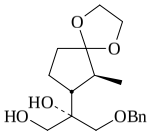
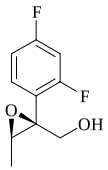
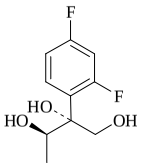
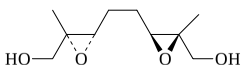
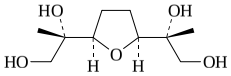
TABLE 3-D. EPOXIDE MIGRATION WITH *O*-NUCLEOPHILE OPENING IN SITU (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
	KOH (0.1%), MeOH, rt, 11 days	 (—)[c]	248
 +  2:1	NaOH, dioxane, 70°	 +  2:1 (—)	256
C_9 	KH, BnOH, THF	 (91)	257
C_{10} 	NaH, BnOH, 100°, 4 h	 (>83)	92, 258



NaOH, H_2O, 1,4-dioxane, 100°



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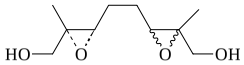
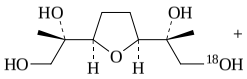
259



NaOH, $H_2{}^{18}O$, 1,4-dioxane, 100°



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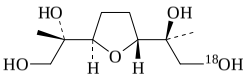
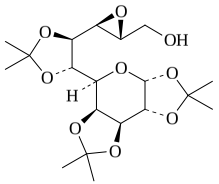
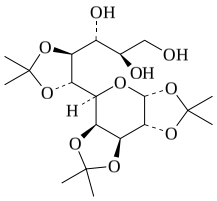


259

meso (38)[a] *d,l* (38)[a]



NaOH, H_2O, 1,4-dioxane, 70°, 24 h



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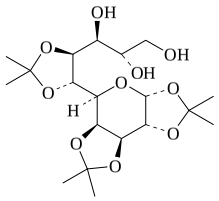
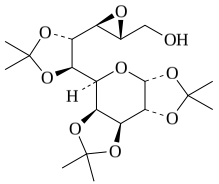
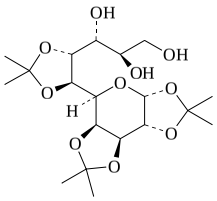


260

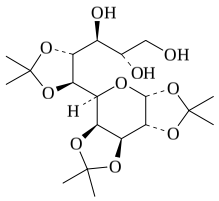
(7) (44)[a]



NaOH, H_2O, 1,4-dioxane, 70°, 24 h



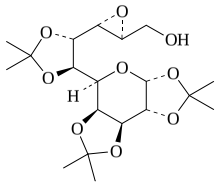
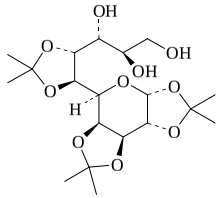
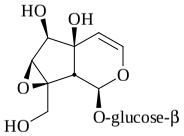
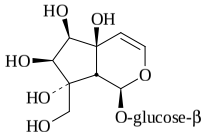
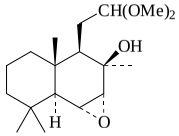
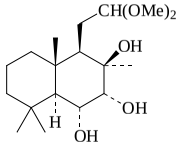
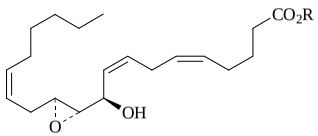
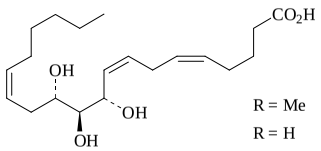
+

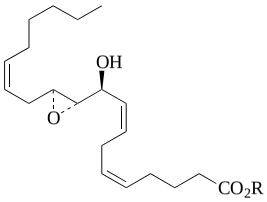


260, 261

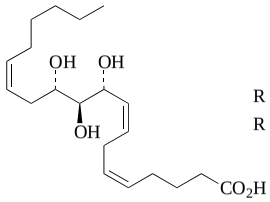
(10) (41)[a]

TABLE 3-D. EPOXIDE MIGRATION WITH *O*-NUCLEOPHILE OPENING IN SITU (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
	$NaOH, H_2O$, 1,4-dioxane, 70°, 22 h	 (63)	260, 261
C_{14} 	$NaOH, H_2O$, 80°, 1 h	 (15)	262
C_{16} 	KOH, H_2O, DMSO, 110°, 2 h	 (12)	263
C_{20} 	LiOH, *t*-BuOH, H_2O, 23°, 9 days	 R = Me (78) R = H (—)	105



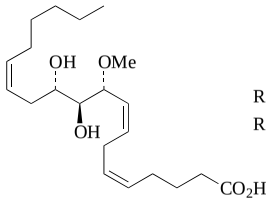
LiOH, *t*-BuOH, H_2O, 23°, 2 days



R = Me (88)
R = H (—)

105

LiOH, MeOH, H_2O, 23°, 3.5 h

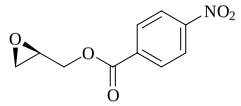
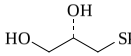
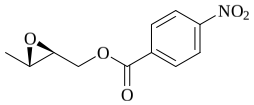
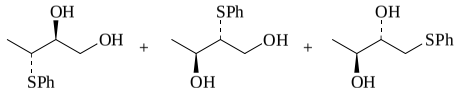
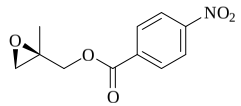
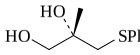
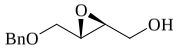
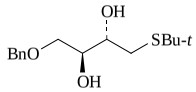
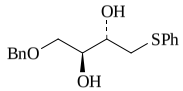
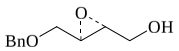
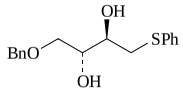


R = Me (67)
R = H (—)

105

[a] This was a product of epoxide migration.
[b] See also Table VII under the same carbon count.
[c] The absolute configuration was not determined. The structure as shown arises from epoxide migration to the 3,4-position followed by nucleophilic opening by the C-1 oxygen. Alternatively, formation of the 1,2-epoxide followed by nucleophilic opening by the C-4 oxygen would give the enantiomer.

TABLE 3-E. EPOXIDE MIGRATION WITH HALIDE AND *S*-NUCLEOPHILE OPENING IN SITU

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_3 	PhSH, NaOH, *t*-BuOH, H_2O	 (93)	38
C_4 	PhSH, NaOH, *t*-BuOH, H_2O	 **I** **II** **III**[a] **I**:**II**:**III** = 29:7:64 (85)	38
	PhSH, NaOH, *t*-BuOH, H_2O	 (87)	38
	*t*-BuSH, NaOH, *t*-BuOH, H_2O, 70–80°, 1–2 h	 (85)	91
	PhSH, NaOH, H_2O, 1,4-dioxane, 65°, 3 h	 (68)[b]	31
	PhSH, NaOH, *t*-BuOH, H_2O, reflux, 3 h	 (52)	98

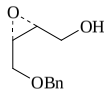
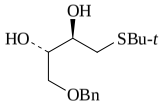
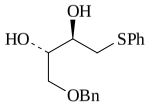
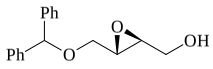
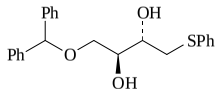
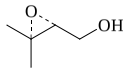
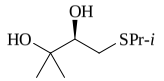
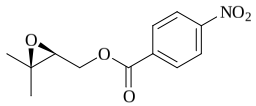
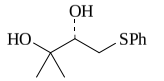
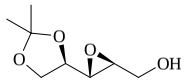
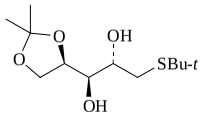
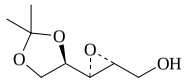
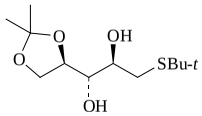
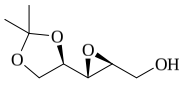
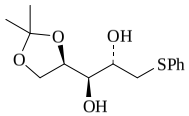
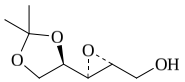
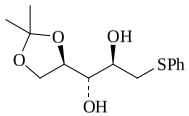
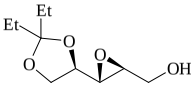
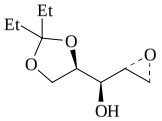
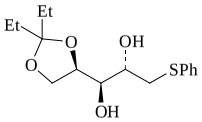
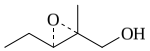
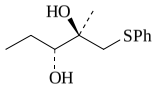
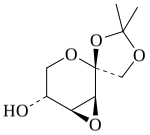
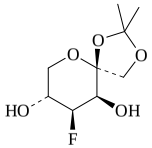
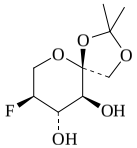
	*t*-BuSH, NaOH, *t*-BuOH, H_2O, 70–80°, 1–2 h		(81)	91
	PhSH, NaOH, H_2O, 1,4-dioxane, 65°, 3 h		(81)	31
	PhSH, NaOH, *t*-BuOH, H_2O, reflux, 3 h		(71)	99
C_5				
	*i*-PrSH, NaOH, *t*-BuOH, EtOH, H_2O, rt, 12 h		(—)	264
	PhSH, NaOH, *t*-BuOH, H_2O		(64)	38
	*t*-BuSH, NaOH, *t*-BuOH, H_2O, 70–80°, 1–2 h		(88)	91
	*t*-BuSH, NaOH, *t*-BuOH, H_2O, 70–80°, 1–2 h		(84)	91

TABLE 3-E. EPOXIDE MIGRATION WITH HALIDE AND *S*-NUCLEOPHILE OPENING IN SITU (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
	PhSH, NaOH, *t*-BuOH, H_2O, 100°, 3 h	 (—)	100, 134
	PhSH, NaOH, *t*-BuOH, H_2O, 100°, 3 h	 (—)	100, 134
	1. *t*-BuSH, NaOH, *t*-BuOH, H_2O 2. NaH, Me_3OBF_4, CH_2Cl_2, 2,6-di-*tert*-butylpyridine	 (57)	265
	PhSH, NaOH, *t*-BuOH, H_2O	 (69)	265
C_6 	KSPh, KOH, H_2O, 25°, 8 h	 (88)	101
	KHF_2, 2-methoxyethanol, reflux	 (19)[a] +  (12)[a]	97

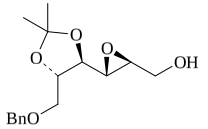
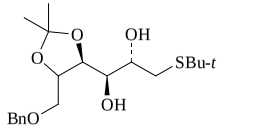
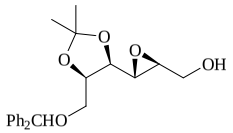
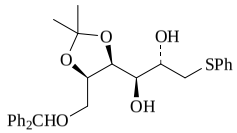
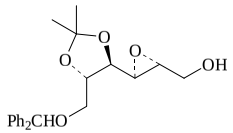
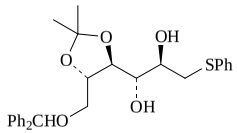
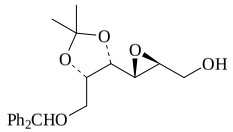
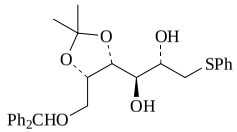
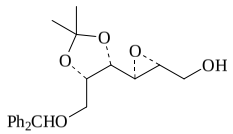
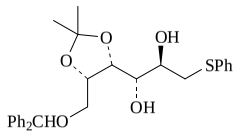
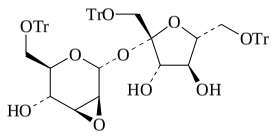
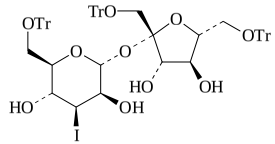
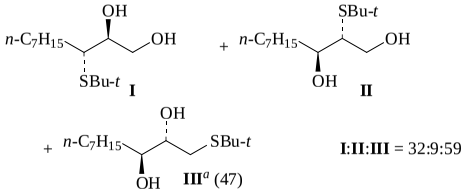
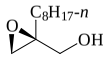
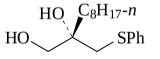
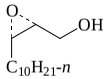
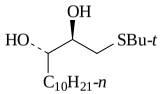
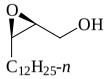
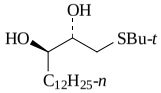
	*t*-BuSH, NaOH, *t*-BuOH, H_2O, 70–80°, 1–2 h		(75)	91
	PhSH, NaOH, *t*-BuOH, H_2O, reflux, 3 h		(79)	99
	PhSH, NaOH, *t*-BuOH, H_2O, reflux, 3 h		(86)	99
	PhSH, NaOH, *t*-BuOH, H_2O, reflux, 3 h		(72)	99
	PhSH, NaOH, *t*-BuOH, H_2O, reflux, 3 h		(63)	99
	LiI, Et_2O, 3–4 days		(37)	96

TABLE 3-E. EPOXIDE MIGRATION WITH HALIDE AND *S*-NUCLEOPHILE OPENING IN SITU (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{10} 	*t*-BuSH, NaOH, *t*-BuOH, H_2O, 70–80°, 1–2 h	 **I** + **II** **I**:**II**:**III** = 32:9:59	91
		+ **III**[a] (47)	
C_{11} 	PhSH, $NaBH_4$, EtOH, rt, 2 h	 (81)	102
C_{13} 	*t*-BuSH, NaOH, *t*-BuOH, H_2O, 70–80°, 1–2 h	 (65)[c]	91
C_{15} 	*t*-BuSH, NaOH, *t*-BuOH, H_2O	 (81)	103

[a] This was a product of epoxide migration.
[b] Approximately 15% of a mixture of other isomers was also isolated.
[c] Approximately 32% of a mixture of other isomers was also isolated.

TABLE 4. EPOXIDE MIGRATION WITH ELECTROPHILIC TRAPPING IN SITU

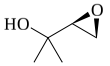
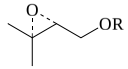
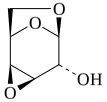
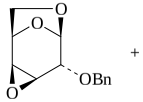
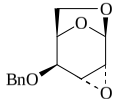
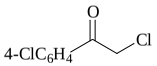
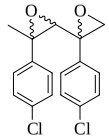
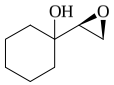
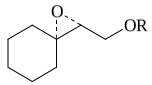
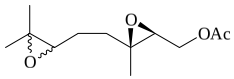
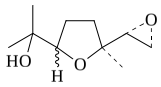
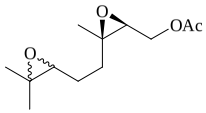
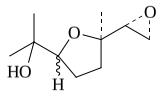
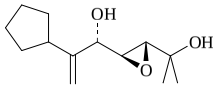
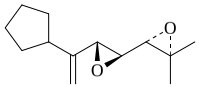
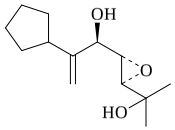
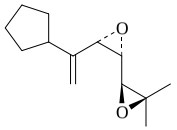
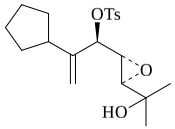
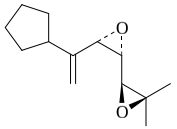
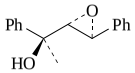
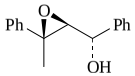
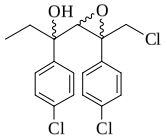
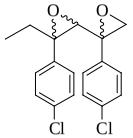
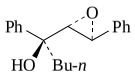
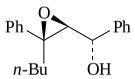
	Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_5		1. NaH, THF 2. RBr	 R=Bn, $CH_2CH=CH_2$ (—)	112
C_6	 β-D-galacto	1. NaH, THF, rt, 5 h 2. BnBr, NBu_4I, rt, 12 h	 β-D-galacto (10) +  β-D-gulo (70)[a]	80
C_8		1. MeMgBr 2. KOH, MeOH	 (—)	188
		1. NaH, THF 2. MeI or allyl bromide	 R=Me, $CH_2C=CH_2$ (—)	112
C_{10}		$NaOH, H_2O$, rt, 2 h	 (54)	115
		$NaOH, H_2O$, rt, 2 h	 (66)	115

TABLE 4. EPOXIDE MIGRATION WITH ELECTROPHILIC TRAPPING IN SITU (*Continued*)

	Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{13}		1. MsCl, py 2. *t*-BuOK, *t*-BuOH, rt, 1 h		(83)	114
		1. MsCl, py 2. *t*-BuOK, *t*-BuOH, rt, 1 h		(80)	114
		*t*-BuOK, *t*-BuOH, rt, 1 h		(55)	114
C_{16}		1. TBDMSCl, imidazole, DMF 2. H_2O		(69)	113
C_{18}		KOH, MeOH, rt		(75)	188
C_{19}		1. TMSCl, imidazole, DMF 2. H_2O		(80)	113

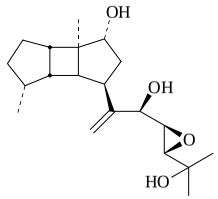
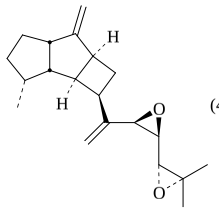
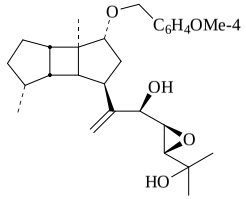
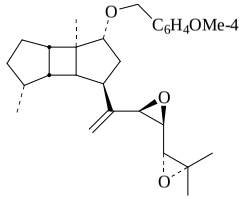
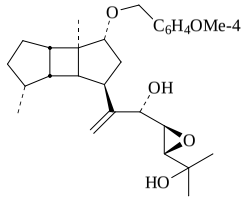
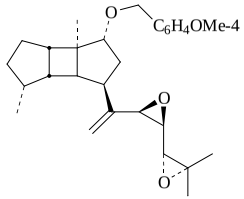
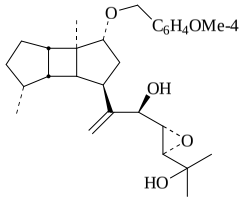
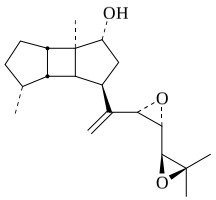
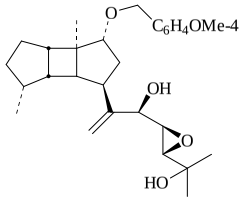
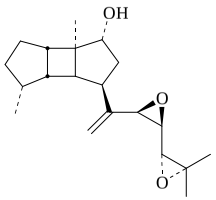
C_{20} 	1. $Zn(OTs)_2$, DEAD, PPh_3, CH_2Cl_2 2. *t*-BuOK, DMF		(46)	114
	1. $Zn(OTs)_2$, DEAD, PPh_3, CH_2Cl_2 2. *t*-BuOK, *t*-BuOH		(68)	114
	1. Ms_2O, DMAP, CH_2Cl_2 2. *t*-BuOK, *t*-BuOH, rt, 1 h		(73)	114

TABLE 4. EPOXIDE MIGRATION WITH ELECTROPHILIC TRAPPING IN SITU (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
	1. Ms_2O, DMAP, py, CH_2Cl_2 2. *t*-BuOK, *t*-BuOH 3. DDQ	 (51)	266
	1. $Zn(OTs)_2$, DEAD, PPh_3, benzene 2. *t*-BuOK, DMF 3. DDQ, CH_2Cl_2	 (58)	266

[a] This was a product of epoxide migration.

TABLE 5-A. AZA-PAYNE REARRANGEMENTS

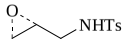
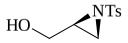
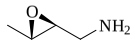
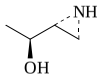
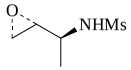
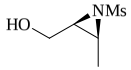
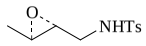
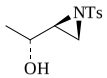
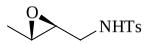
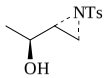
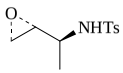
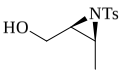
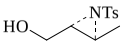
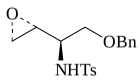
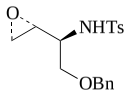
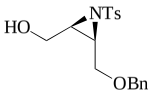
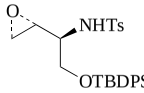
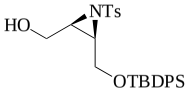
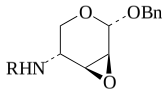
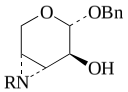
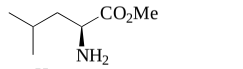
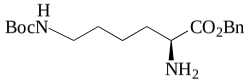
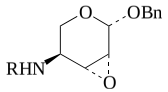
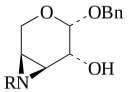
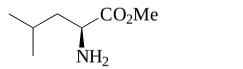
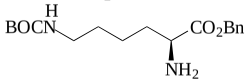
	Oxirane (**I**)	Aziridine (**II**)	Initial Compound	Conditions	Final Mixture **I**:**II**	Final Mixture Yield (%)	Refs.
C_3			**II**	NaH, THF, HMPA, rt 1 h	—	**I** (65)	57
C_4			**I**	*n*-BuLi, $AlMe_3$, THF, –80 to 0°	—	**II** (69)	61
			I	*t*-BuOK, *n*-BuLi, *n*-hexane, THF, –78°	—	**II** (85)	57
			**II**	NaH, THF, HMPA, 0°, 2 h	—	**I** (80)	57
			**II**	KH, CH_2Cl_2, 0°, 4 h	—	**I** (77)	57
			**II**	KH, CH_2Cl_2, 0°, 4 h	—	**I** (76)	57
			**II**	NaH, THF, HMPA, –78° to rt, 18 h	—	**I** (92)	64
			II	KH, CH_2Cl_2 or toluene, 0°, 1 h	—	**I** (99)	57
			II	NaOH, *t*-BuOH, H_2O, 0°, 18 h	70:30	(—)	57
			**II**	NaH, THF, HMPA, –78° to rt, 18 h	—	**I** (87)	64
			II	KH, THF, HMPA, 0°, 30 min	—	**I** (92)	57
			**II**	KH, THF, HMPA, 0°, 1 h	—	**I** (95)	57

TABLE 5-A. AZA-PAYNE REARRANGEMENTS (*Continued*)

Oxirane (**I**)	Aziridine (**II**)	Initial Compound	Conditions	Final Mixture **I**:**II**	Final Mixture Yield (%)	Refs.
		**II**	NaH, THF, HMPA, rt, 2 h	—	**I** (97)	57
		**II**	*t*-BuOLi, THF, HMPA	—	**I** (95)	20
C_5  α-D-lyxo	 α-D-arabino	**I**[a]	RNH_2, DMF, rt, 5 h			116
			RNH_2 	88:12	(89)	
				82:18	(55)	
 β-L-lyxo	 β-L-arabino	**I**[a]	RNH_2, DMF, rt, 5 h			116
			RNH_2 	87:13	(68)	
				83:17	(52)	

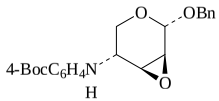
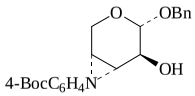
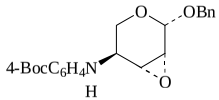
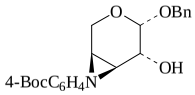
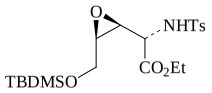
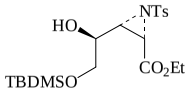
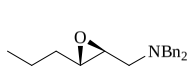
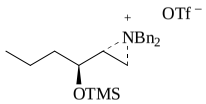
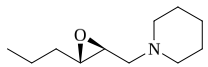
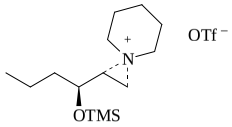
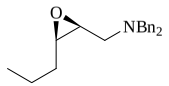
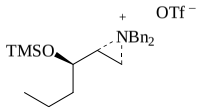
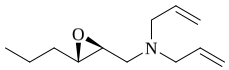
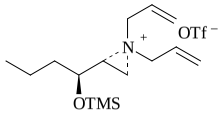
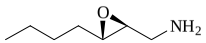
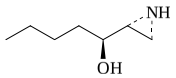
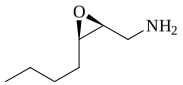
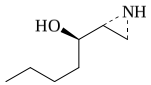
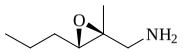
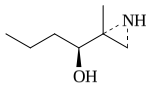
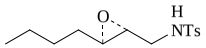
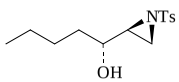
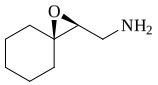
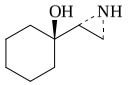
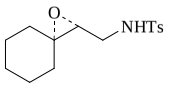
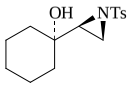
 α-D-lyxo	 α-D-arabino	**I**	BF_3•Et_2O, $TMSN_3$, rt, 1.5 h	—	**II** (60)	60
 β-L-lyxo	 β-L-arabino	**I**	BF_3•Et_2O, $TMSN_3$, rt, 1.5 h	—	**II** (53)	60
		**II**	Py, DMSO	—	**I** (64)	118
C_6 		**I**	TMSOTf, $CDCl_3$, –40° to rt	0:100	(—)	62
		**I**	TMSOTf, $CDCl_3$, –40° to rt	0:100	(—)	62
		**I**	TMSOTf, CH_2Cl_2, –78°	0:100	(—)[b]	62

TABLE 5-A. AZA-PAYNE REARRANGEMENTS (*Continued*)

	Oxirane (**I**)	Aziridine (**II**)	Initial Compound	Conditions	Final Mixture **I**:**II**	Final Mixture Yield (%)	Refs.
			**I**	TMSOTf, $CDCl_3$, –40° to rt	0:100	(—)	62
			II	K_2CO_3, MeOH	100:0	**I** (87)	
C_7			**I**	*n*-BuLi, $AlMe_3$, THF, –80 to 0°	—	**II** (72)	61
			I	*t*-BuOK, *n*-BuLi, *n*-hexane, THF, –78°	—	**II** (85)	57
			**I**	*n*-BuLi, $AlMe_3$, THF, –80 to 0°	—	**II** (75)	61
			**I**	*t*-BuOK, *n*-BuLi, *n*-hexane, THF, 0°, 3 h	—	**II** (40)	57
			**II**	KH, THF, 0°, 2 h	—	**I** (88)	57
C_8			**I**	*t*-BuOK, *n*-BuLi, *n*-hexane, THF, –78°	—	**II** (96)	57
			**II**	NaOH, *t*-BuOH, H_2O, 0°, 18 h	98:2	(100)	57
			II	KH, THF, rt, 18 h	—	**I** (99)	

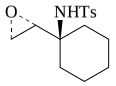
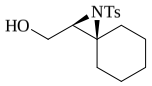
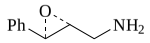
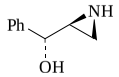
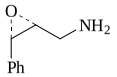
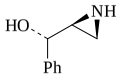
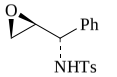
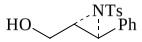
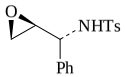
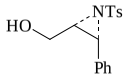
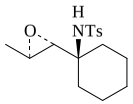
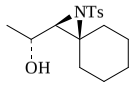
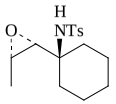
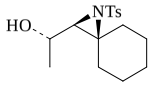
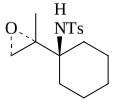
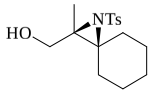
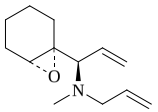
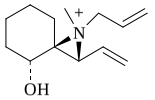
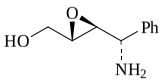
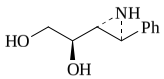
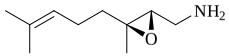
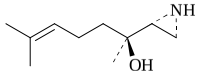
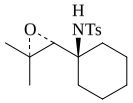
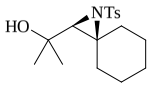
			**I**	NaOH, H_2O, brief heating	—	**II** (90)	63
C_9			**I**	*n*-BuLi, $AlMe_3$, THF, –80° to 0°	—	**II** (73)	61
			I	*t*-BuOK, *n*-BuLi, *n*-hexane, THF, –78°	—	**II** (80)	57
			**I**	*n*-BuLi, $AlMe_3$, THF, –80° to 0°	—	**II** (78)	61
			**II**	KH, THF, HMPA, 0°, 1.5 h	—	**I** (91)	57
			**II**	KH, THF, HMPA, 0°, 1.5 h	—	**I** (94)	57
			II	NaOH, *t*-BuOH, H_2O, 0°, 18 h	39:61	(100)	57
			**I**	NaOH, H_2O, reflux, 5 min	—	**II** (85)	63
			**I**	NaOH, H_2O, reflux, 5 min	—	**II** (81)	63
			**I**	NaOH, H_2O, reflux, 5 min	—	**II** (80)	63

TABLE 5-A. AZA-PAYNE REARRANGEMENTS (*Continued*)

Oxirane (**I**)	Aziridine (**II**)	Initial Compound	Conditions	Final Mixture **I**:**II**	Final Mixture Yield (%)	Refs.
		**II**[c]	NaH, MeI, THF, 0°, 12 h	—	**I** (14)	117
C_{10} 		**I**	$Ti(OPr\text{-}i)_4$, THF, 0°, 3 h	—	**II** (63)	59
		**I**	*t*-BuOK, *n*-BuLi, *n*-hexane, THF, –78°	—	**II** (88)	57
		**I**	NaOH, H_2O, reflux, 5 min	—	**II** (93)	63

[a] The starting material in this reaction was the 4-*O*-triflate, which was displaced by the amine to produce **I** directly and **II** indirectly.

[b] The product was contaminated by azetidinium salt formed by reaction at C-3.

[c] The starting material in this reaction was the free base, which was treated with methyl iodide to form **II** in situ.

TABLE 5-B. AZA-PAYNE REARRANGEMENT WITH NUCLEOPHILIC OPENING IN SITU

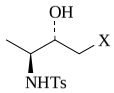
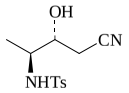
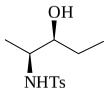
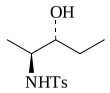
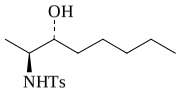
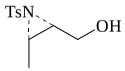
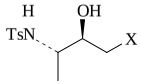
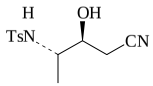
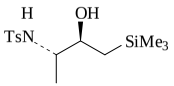
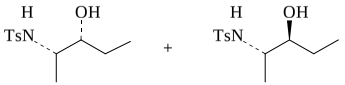
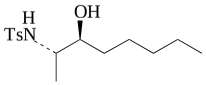
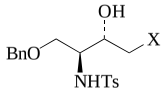
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
	1. KH, THF, 0°, 1 h		124
	2. $Me_2Cu(CN)Li_2$•2LiBr, THF, Et_2O, –78°, 0.5 h	X = Me (90)	
	2. *n*-$Bu_2Cu(CN)Li_2$, *n*-hexane, THF, –78 to 0°, 2 h	X = *n*-Bu (88)	
	2. PhSH, THF, rt, 2 h	X = SPh (88)	
	2. *t*-BuSH, THF, rt, 2 h	X = SBu-*t* (59)	
	1. KH, THF, 0°, 1 h 2. Me_3SiCN, $Yb(CN)_3$ (cat.), THF, hexane, rt, 3 h 3. *n*-Bu_4NF, THF, 0°, 15 min	 (86)	124
	MeCu(CN)Li•LiBr, THF, Et_2O, –78° to rt, 18 h	 (39) +  (53)	57, 64
	n-BuCu(CN)Li•2LiCl, *n*-hexane, THF	 (91)	57

TABLE 5-B. AZA-PAYNE REARRANGEMENT WITH NUCLEOPHILIC OPENING IN SITU (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
	1. KH, THF, 0°, 1 h		123, 124
	2. $Me_2Cu(CN)Li_2$•2LiBr, THF, Et_2O, –78°, 0.5 h	X = Me (99)	
	2. *n*-$Bu_2Cu(CN)Li_2$, *n*-hexane, THF, –78 to 0°, 2 h	X = *n*-Bu (89)	
	2. (*n*-$Bu_3Sn)_2Cu(CN)Li_2$, THF, hexane, –10°, 1 h	X = *n*-Bu_3Sn (68)	
	2. (*n*-$Bu_2N)_2Cu(CN)Li_2$, THF, hexane, 0°, 1.5 h	X = *n*-Bu_2N (91)	
	2. PhSH, THF, rt, 2 h	X = SPh (91)	
	2. *t*-BuSH, THF, rt, 2 h	X = SBu-*t* (70)	
	1. KH, THF, 0°, 1 h 2. Me_3SiCN, $Yb(CN)_3$ (cat.), THF, hexane, rt, 3 h 3. *n*-Bu_4NF, THF, 0°, 15 min	 (90)	123, 124
	1. KH, THF 0°, 1 h 2. $(Me_3Si)_2Cu(CN)Li_2$	 (58)	123
	MeCu(CN)Li•LiBr, THF, Et_2O, –78° to rt, 18 h	 (55) + (36)	57, 64

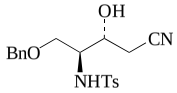
n-BuCu(CN)Li•2LiCl, *n*-hexane, THF 

(41) 57

1. KH, THF, 0°, 1 h 

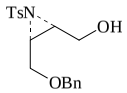
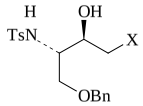
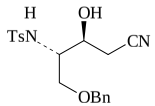
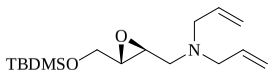
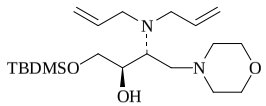
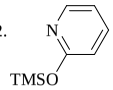
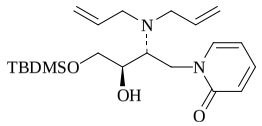
	X	(%)	
2. $Me_2Cu(CN)Li_2$•2LiBr, THF, Et_2O, –78°, 0.5 h	Me	99	124
2. $Bu_2Cu(CN)Li_2$, THF, Et_2O, –78 to 0°, 2 h	*n*-Bu	91	123, 124
2. (*n*-$C_{14}H_{29})_2Cu(CN)Li_2$, THF, –78°, 2 h	*n*-$C_{14}H_{29}$	93	124
2. (*n*-$Bu_2N)_2Cu(CN)Li_2$, THF, hexane, 0°, 1.5 h	*n*-Bu_2N	88	123, 124
2. PhSH, THF, rt, 2 h	SPh	94	123, 124
2. *t*-BuSH, THF, rt, 2 h	SBu-*t*	95	123, 124

1. KH, THF, 0°, 1 h
2. Me_3SiCN, cat. $Yb(CN)_3$, THF, hexane, rt, 3 h
3. *n*-Bu_4NF, THF, 0°, 15 min



(95) 123, 124

TABLE 5-B. AZA-PAYNE REARRANGEMENT WITH NUCLEOPHILIC OPENING IN SITU (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
	1. KH, THF, 0°, 1 h 2. $Me_2Cu(CN)Li_2$•2LiBr, THF, Et_2O, –78°, 0.5 h 2. (n-$C_{14}H_{29})_2Cu(CN)Li_2$, THF, –78°, 2 h 2. ($n$-$Bu_3Sn)_2Cu(CN)Li_2$, THF, hexane, –10°, 1 h 2. (n-$Bu_2N)_2Cu(CN)Li_2$, THF, hexane, 0°, 1.5 h 2. PhSH, THF, rt, 2 h	 X (%) Me 98 n-$C_{14}H_{29}$ 90 n-Bu_3Sn 42 n-Bu_2N 88 SPh 92	123, 124
	1. KH, THF, 0°, 1 h 2. TMSCN, $Yb(CN)_3$ (cat), THF, hexane, rt, 3 h 3. n-Bu_4NF, THF, 0°, 15 min	 (85)	124
	1. TMSOTf, CH_2Cl_2, –78° 2. morpholine, –78° to rt 3. K_2CO_3, MeOH, rt	 (59)	62
	1. TMSOTf, CH_2Cl_2, –78° 2.  , –78° to rt 3. K_2CO_3, MeOH, rt	 (79)	62

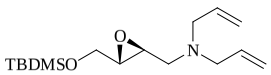
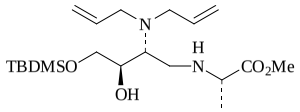
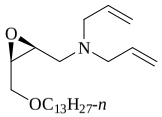
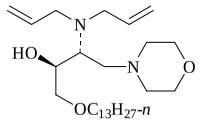
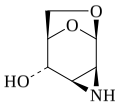
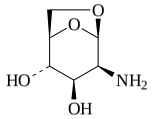
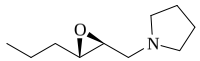
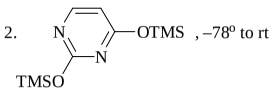
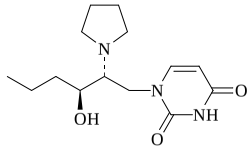
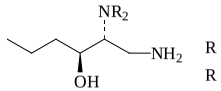
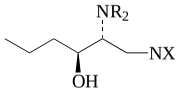
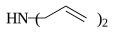
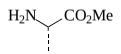
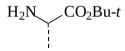
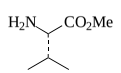
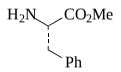
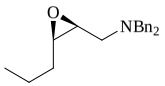
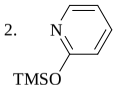
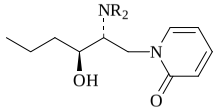
	1. TMSOTf, CH_2Cl_2, –78° 2. H_2N–CH(CO_2Me)– , –78° to rt 3. K_2CO_3, MeOH, rt		(74)	19, 121
	1. TMSOTf, CH_2Cl_2, –78° 2. morpholine, –78° to rt 3. K_2CO_3, MeOH, rt		(61)	62
C_6  β-D-manno	KOH, H_2O, 90–100°, 6 h	 β-D-manno	(32)	122
	1. TMSOTf, CH_2Cl_2, –78° 2.  , –78° to rt 3. K_2CO_3, MeOH, rt		(79)	62
	1. TMSOTf, CH_2Cl_2, –78° 2. NH_3 (*l*)		R = Bn (65) R = allyl (54)	62

TABLE 5-B. AZA-PAYNE REARRANGEMENT WITH NUCLEOPHILIC OPENING IN SITU (*Continued*)

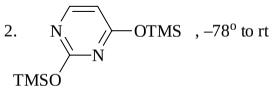
Substrate	Conditions	Product(s) and Yield(s) (%)		Refs.
	1. TMSOTf, CH_2Cl_2, –78° 2. HNX, –78° to rt 3. K_2CO_3, MeOH, rt			
	HNX	R = allyl (%)	R = Bn (%)	
	H_2NPr-*i*	47	47	62, 120
	H_2NBu	—	44	62, 120
		88	67	62
		66	60	62, 120
		90	92	62, 120
		—	87	19, 121
		77	86	19, 121
		84	88	19, 121
		85	90	19, 121
		91	88	19, 121

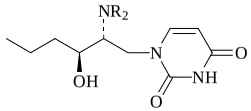


1. TMSOTf, CH_2Cl_2, –78°
2.  , –78° to rt
3. K_2CO_3, MeOH, rt

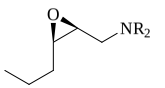


R = Bn	(93)	62, 120
R = allyl	(83)	62, 120

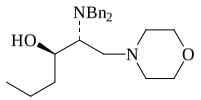
1. TMSOTf, CH_2Cl_2, –78°
2.  , –78° to rt
3. K_2CO_3, MeOH, rt



R = Bn	(89)	62, 120
R = allyl	(91)	62, 120

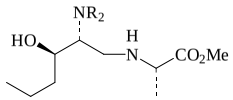


1. TMSOTf, CH_2Cl_2, –78°
2. morpholine, –78° to rt
3. K_2CO_3, MeOH, rt

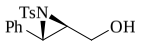


(58) 62

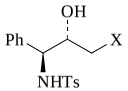
1. TMSOTf, CH_2Cl_2, –78°
2. H_2N–CH(CO_2Me)– , –78° to rt
3. K_2CO_3, MeOH, rt



R = Bn	(62)	19, 121
R = allyl	(57)	19, 121

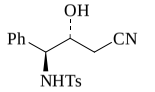
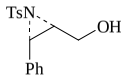
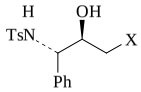
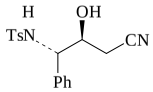
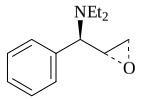
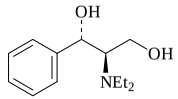
C_9 

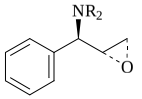
1. KH, THF, 0°, 1 h



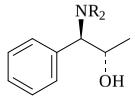
X	(%)	
2. $Me_2Cu(CN)Li_2$•2LiBr, THF, Et_2O, –78°, 0.5 h		
Me	93	123, 124
2. PhSH, THF, rt, 2 h		
SPh	64	124

TABLE 5-B. AZA-PAYNE REARRANGEMENT WITH NUCLEOPHILIC OPENING IN SITU (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
	1. KH, THF, 0°, 1 h 2. TMSCN, $Yb(CN)_3$ (cat.), THF, hexane, rt, 3 h 3. *n*-Bu_4NF, THF, 0°, 15 min	 (67)	123, 124
	1. KH, THF, 0°, 1 h		
		X (%)	
	2. $Me_2Cu(CN)Li_2$•2LiBr, THF, Et_2O, –78°, 0.5 h	Me 75	124
	2. *n*-$Bu_2Cu(CN)Li_2$, *n*-hexane, THF, –78 to 0°, 2 h	Bu 94	123, 124
	2. (*n*-$Bu_3Sn)_2Cu(CN)Li_2$, THF, hexane, –10°, 1 h	*n*-Bu_3Sn 52	123, 124
	2. (*n*-$Bu_2N)_2Cu(CN)Li_2$, THF, hexane, 0°, 1.5 h	*n*-Bu_2N 94	123, 124
	2. PhSH, THF, rt, 2 h	SPh 89	124
	1. KH, THF, 0°, 1 h 2. TMSCN, $Yb(CN)_3$ (cat.), THF, hexane, rt, 3 h 3. *n*-Bu_4NF, THF, 0°, 15 min	 (85)	123, 124
	SiO_2 chromatography	 (33)	119

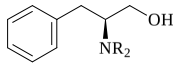


$NaBH_3CN$, $BF_3{\bullet}Et_2O$, THF, reflux

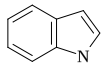
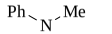
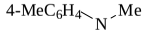
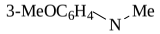
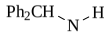


I

+

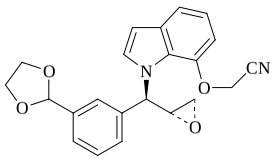


II

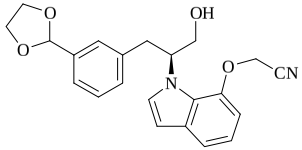
NR_2	**I** (%)	**II** (%)
	0	48
	14	0
	0	48
	27	27
	0	65
	17	39

119

C_{10}



$NaBH_3CN$, $BF_3{\bullet}Et_2O$, THF, reflux, 3.5 h

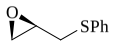
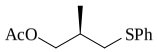
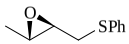
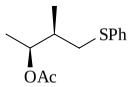
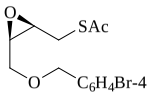
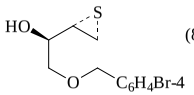
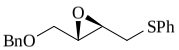
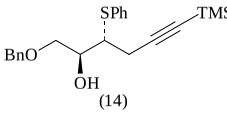
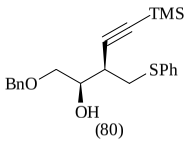
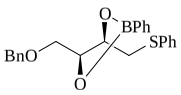
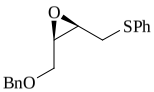
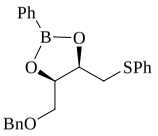


(37)

119

[a] This was the product of an aza-Payne rearrangement.

TABLE 6. REACTIONS INVOLVING THIA-PAYNE REARRANGEMENTS

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_3 	1. $AlMe_3$, hexane, 0°, 30 min 2. Ac_2O, DMAP, py	 (72)	67
C_4 	1. $AlMe_3$, hexane, 0°, 1 h 2. Ac_2O, DMAP, py	 (89)	67
	NH_3, MeOH, 0°, 3 h	 (89)	65
	$Me_2AlC{\equiv}CTMS$, CH_2Cl_2, –78°, 10 min	 (14) +  (80)	68
	$PhB(OH)_2$, 70°, 20 h	 (100)	69
	$PhB(OH)_2$, 70°, 3 h	 (99)	69

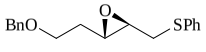
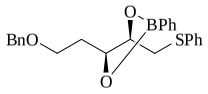
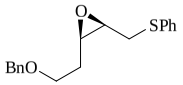
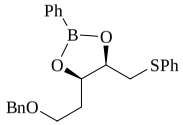
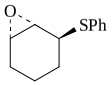
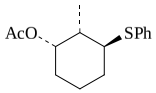
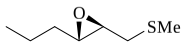
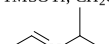
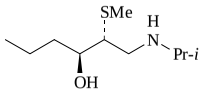
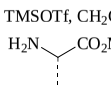
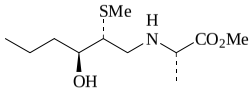
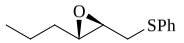
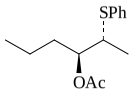
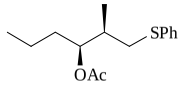
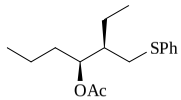
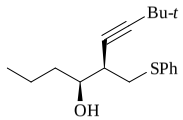
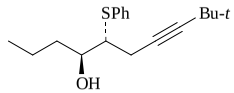
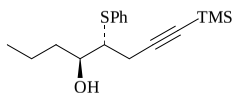
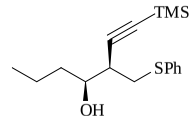
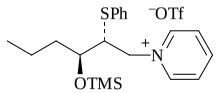
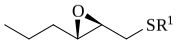
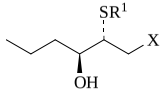
C_5		$PhB(OH)_2$, 70°, 17.5 h		(98)	69
		$PhB(OH)_2$, 70°, 13.5 h		(97)	69
C_6		1. $AlMe_3$, hexane, 0°, 0.6 h 2. Ac_2O, DMAP, py		(74)	67
		1. TMSOTf, CH_2Cl_2, –78°, 10 min 2.  , 0°, 72 h 3. K_2CO_3, H_2O, rt, 3 h		(70)	66, 128
		1. TMSOTf, CH_2Cl_2, –78°, 10 min 2.  , –78°, 4–24 h 3. $NaHCO_3$, H_2O, rt 4. AcOH, MeOH, rt, 3h		(53)	126, 127
		1. $(i\text{-Bu})_2AlH$, hexane, 0°, 1 h 2. Ac_2O, DMAP, py		(86)	67

TABLE 6. REACTIONS INVOLVING THIA-PAYNE REARRANGEMENTS (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
	1. $AlMe_3$, hexane, 0^o, 1 h 2. Ac_2O, DMAP, py	 (92)	67
	1. $AlEt_3$, hexane, 0^o, 1 h 2. Ac_2O, DMAP, py	 (86)	67
	$Et_2AlC{\equiv}CBu\text{-}t$, hexane, 0^o, 2 h	 (8) +  (70)	67
	$Me_2AlC{\equiv}CTMS$, CH_2Cl_2, -78^o, 10 min	 (9) +  (82)	68
	1. TMSOTf, CH_2Cl_2, -78^o 2. py, -78^o to rt	 (99)	66



1. TMSOTf, CH_2Cl_2, –78°, 10 min
2. nucleophile, –78 to 0°, 1–3 days
3. K_2CO_3, MeOH, rt, 45 min



66, 125

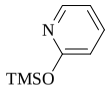
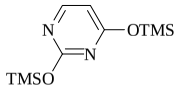
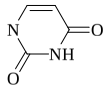
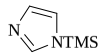
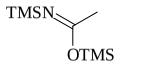
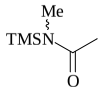
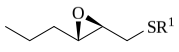
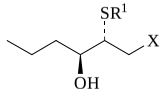
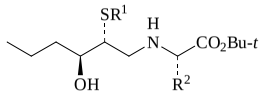
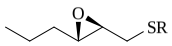
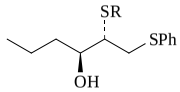
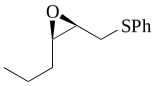
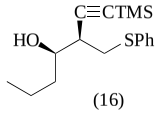
nucleophile	X	(%) R^1 = Me	R^1 = Ph	R^1 = Bn
		85	81	—
		81	75	53
		33	39	—
	NHAc	54	58	51
	NMeAc	44	55	—

TABLE 6. REACTIONS INVOLVING THIA-PAYNE REARRANGEMENTS (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
	1. BF_3•Et_2O, CH_2Cl_2, –78°, 10 min 2. TMSX, –78 to 0°, 3 days 3. K_2CO_3, MeOH, rt, 45 min		66, 125
		X:  — R^1 = Me: 47 %; R^1 = Ph: 40 %	
		X:  — R^1 = Me: 44 %; R^1 = Ph: —	
		X:  — R^1 = Me: 37 %; R^1 = Ph: 33 %	
	1. TMSOTf, CH_2Cl_2, –78°, 10 min 2. H_2N–CH(R^2)–CO_2Bu-*t*, –78°, 4–24 h 3. $NaHCO_3$, H_2O, rt 4. AcOH, MeOH, rt, 3 h		126, 127
		R^2 (Me (ala): R^1 = Me 54 %, R^1 = Ph 48 %); (*i*-Bu (leu): 54 %, 58 %); ($PhCH_2$ (phe): 49 %, —)	
	1. TMSOTf, CH_2Cl_2, –78° 2. TMSSPh, –78°, 2 days 3. NEt_3, –78°, 1 h 4. K_2CO_3, MeOH, rt, 2 h		129
		R: Me 30 %; *i*-Bu 70 %; *n*-Bu 64 %; Ph 46 %	



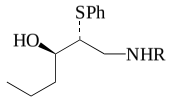
$Me_2AlC{\equiv}CTMS$, CH_2Cl_2, –78°, 10 min



(16) + (77)

68

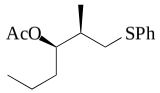
1. TMSOTf, CH_2Cl_2, –78°, 10 min
2. R–N=CH–C_6H_4OMe-4, 0°, 72 h
3. K_2CO_3, MeOH, rt, 3 h



R	(%)
i-Pr	57
Ph	66
Bn	46

66, 128

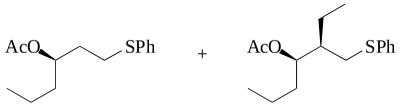
1. $AlMe_3$, hexane, 0°, 1 h
2. Ac_2O, DMAP, py



(92)

67

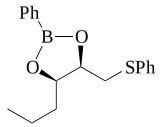
1. $AlEt_3$, hexane, 0°, 2 h
2. Ac_2O, DMAP, py



(40) + (43)[a]

67

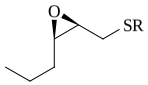
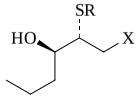
$PhB(OH)_2$, 70°, 21 h

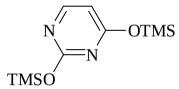
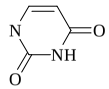
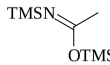


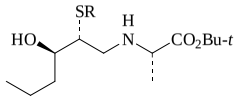
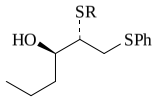
(98)

69

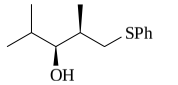
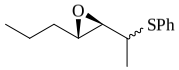
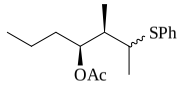
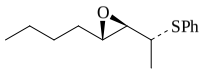
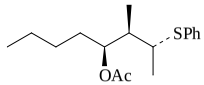
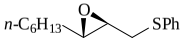
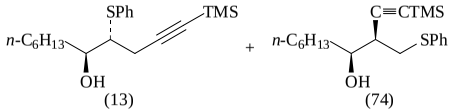
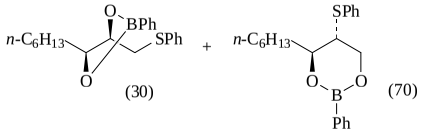
TABLE 6. REACTIONS INVOLVING THIA-PAYNE REARRANGEMENTS (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
	1. TMSOTf, CH_2Cl_2, –78°, 10 min 2. nucleophile, –78 to 0°, 1–3 days 3. K_2CO_3, MeOH, rt, 45 min		66, 125

nucleophile	X	R = Me (%)	R = Ph (%)
		68	55
	NHAc	44	40

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
	1. TMSOTf, CH_2Cl_2, –78°, 10 min 2. H_2N–CH(CO_2Bu-*t*)–, –78°, 4–24 h 3. $NaHCO_3$, H_2O, rt 4. AcOH, MeOH, rt, 3 h	 R = Me (44) R = Ph (43)	126, 127 126, 127
	1. TMSOTf, CH_2Cl_2, –78° 2. TMSSPh, –78°, 2 days 3. NEt_3, –78°, 1 h 4. K_2CO_3, MeOH, rt, 2 h		129

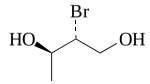
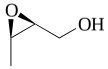
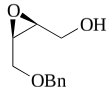
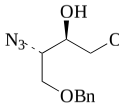
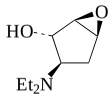
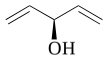
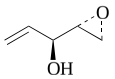
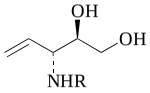
R	(%)
Me	50
i-Bu	56
n-Bu	33
Ph	55

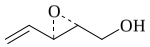
C_7		$AlMe_3$, hexane, 0^o, 30 min	 (96)	67
		1. $AlMe_3$, hexane, 0^o, 0.6 h 2. Ac_2O, DMAP, py	 $(91)^b$	67
C_8		1. $AlMe_3$, hexane, 0^o, 30 min 2. Ac_2O, DMAP, py	 (90)	67
C_9		$Me_2AlC{\equiv}CTMS$, CH_2Cl_2, –78°, 10 min	 (13) + (74)	68
		$PhB(OH)_2$, $BF_3{\bullet}Et_2O$, 60^o, 48 h	 (30) + (70)	69

[a] This was a product of the thia-Payne rearrangement.

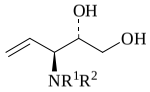
[b] A roughly 3:1 mixture of diastereomers was retained throughout the reaction.

TABLE 7. CONDITIONS NOT LEADING TO EPOXIDE MIGRATION[a]

	Substrate	Conditions	Product(s) and Yield(s) (%)	Related Table[b]	Refs.
C_4		K_2CO_3, MeOH, 0° to rt, 8 h	 (65)	I-B	41
		DBU, THF 0° to rt, 18 h	(80)		41
		NaN_3, $LiClO_4$, NH_4ClO_4, MeCN, MeOH	 (23) + (61)	III-C	93
C_5		Et_2NH, H_2O, 50°, 4 h	 (32)	II-B	221
		EtMgBr, THF, –70° to rt	 (80)	II-B[c]	267
		1. $Ti(OPr\text{-}i)_4$ (1 eq), $t\text{-}BuO_2H$, L-(+)-DET, CH_2Cl_2, –20° 2. acetone (aq.), distillation	 (50–60)	I-B	106
				III-C	108
					109
		NH_3, H_2O, rt, 2–3 d	R: H — (%): 100		
		(*R*)-$H_2NCH(Me)Ph$, 100°, 27 h	R: (*R*)-CH(Me)Ph — (%): 90		



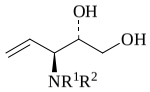
R^1R^2NH, $Ti(OPr\text{-}i)_4$, CH_2Cl_2, rt, 1–4 d



III-C 109

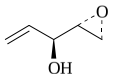
R^1	R^2	(%)
H	Bn	50
H	*i*-Pr	74
H	(*R*)-CH(Me)Ph	90
H	*t*-Bu	91
H	Ph	76
i-Pr	*i*-Pr	83
Bn	Bn	87

R^1R^2NH, rt, 2–4 d

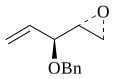


III-C 109

R^1	R^2	(%)
H	H	77
H	(*S*)-CH(Me)Ph	80
Me	Me	98



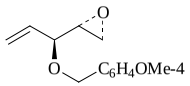
BnBr, NaH, *n*-Bu_4NI, THF, –10°



(80) I-A 268

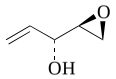
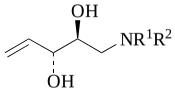
BnBr, NaH, *n*-Bu_4NI, THF, rt (—) 197

4-$MeOC_6H_4CH_2Br$, NaH, THF, 0°

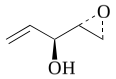
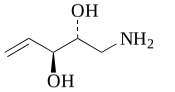
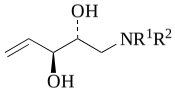


(94) IV 269

TABLE 7. CONDITIONS NOT LEADING TO EPOXIDE MIGRATION (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Related Table[b]	Refs.
	R^1R^2N, rt, 1 d		III-C	270, 271

R^1	R^2	(%)
H	H	78
H	(*R*)-CH(Me)Ph	93
H	(*S*)-CH(Me)Ph	78

Substrate	Conditions	Product(s) and Yield(s) (%)	Related Table[b]	Refs.
	NH_3 (*l*), –78° to rt	 (100)	III-C	108, 271
	NH_3, H_2O, rt, 2 d	(100)		270
	R^1R^2N, rt, 1–5 d		III-C	108, 270

R^1	R^2	(%)
H	Bn	83
H	(*R*)-CH(Me)Ph	96
H	(*S*)-CH(Me)Ph	91
H	*i*-Pr	90
H	*t*-Bu	100
H	Ph	90
Me	Me	96
i-Pr	*i*-Pr	74

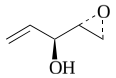
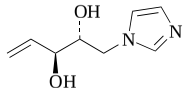
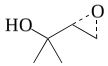
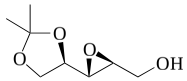
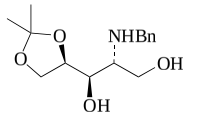
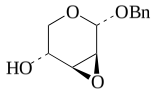
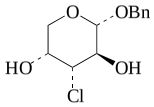
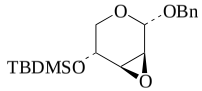
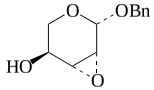
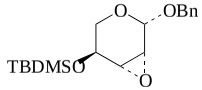
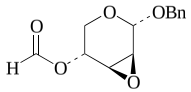
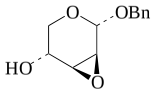
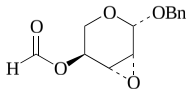
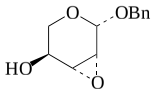
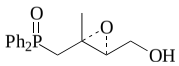
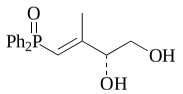
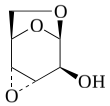
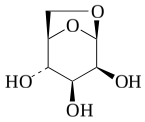
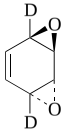
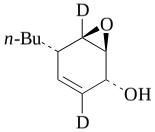
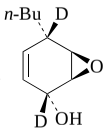
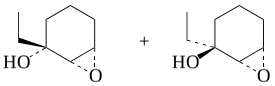
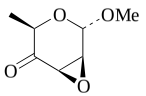
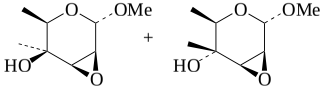
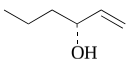
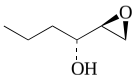
	Imidazole, Ti(OPr-*i*)$_4$, CH_2Cl_2, rt, 5 d		(54)	III-C	270
	NaH, THF, 10°, 1.5 h	—[d]		I-A	3
	$BnNH_2$, Et_3Al, CH_2Cl_2, 25°		(—)	III-C	272
	$PdCl_2(PhCN)_2$, C_6H_6, reflux, 6–48 h		(50)	—	273
	TBDMSCl, imidazole, DMF, 35°, 50 min		(93)	II-A	196
	TBDMSCl, imidazole, DMF, 35°, 50 min		(98)	II-A	196
	NaOH, DMF, H_2O, rt		(78)	II-A	196
	NaOH, DMF, H_2O, rt		(86)	II-A	196

TABLE 7. CONDITIONS NOT LEADING TO EPOXIDE MIGRATION (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Related Table[b]	Refs.
	NaOH, H_2O, *t*-BuOH	 + other isomers (88)	I-A	274
C_6  β-D-altro	KOH, H_2O, 100°, 5 h	 (—) β-D-manno	III-D	111
	*n*-BuLi	 not  (—)	II-B	275
	1. EtMgBr, THF, –70°, 15 min 2. NH_4Cl, H_2O	 (16)	II-B	222
	1. MeLi, THF, Et_2O, –78° 2. H_2O, HOAc, –25°	 α-D-talo (80) α-D-manno (11)	II-B	70
	$Ti(OPr\text{-}i)_4$ (5 mol%), *t*-BuO_2H, L-(–)-DET, CH_2Cl_2, –20°	 (78)	I-B	213

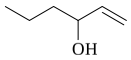
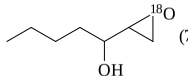
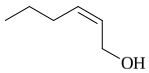
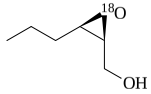
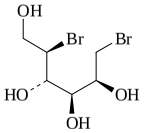
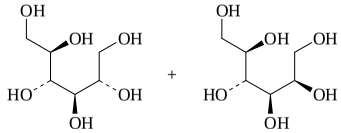
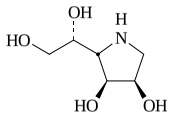
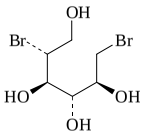
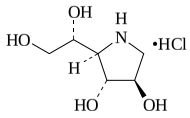
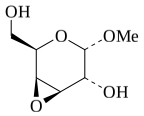
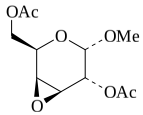
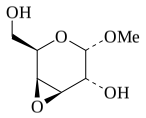
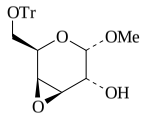
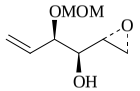
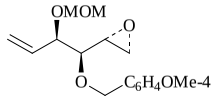
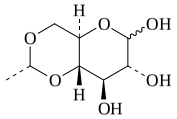
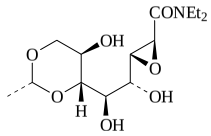
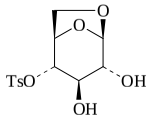
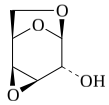
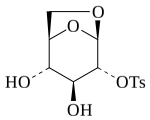
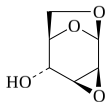
	1. Ag_2O, I_2, THF, $^{18}OH_2$ 2. DBU, CH_2Cl_2, THF, rt, 24 h		(72)	I-B	276
	1. Ag_2O, I_2, THF, $^{18}OH_2$ 2. DBU, CH_2Cl_2, THF, rt, 24 h		(70)	I-B	276
	K_2CO_3, H_2O, 20^o, 9 days		(31)[e] + (69)	I-B	45
	NH_3, H_2O, rt, 3 h		(69)	III-D	43
	1. NH_3, H_2O, rt, 2 h 2. HCl		(55)	III-D	44
	Ac_2O, py, rt, 24 h		(97)	II-A	53

TABLE 7. CONDITIONS NOT LEADING TO EPOXIDE MIGRATION (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Related Table[b]	Refs.
	TrCl, py, rt, 40 h	 (85)	II-A	53
	NaH, 4-$MeOC_6H_4CH_2Br$	 (84)	I-A	277, 278
	1. $Me_2\overset{+}{S}\overset{-}{C}HCONEt_2$, THF, 0°, 2 days 2. rt, 1 d	 (69)	III-D	248
 β-D-gluco	Amberlite IRA 400 OH^-, MeOH, rt, 5 min	 (98) β-D-galacto	II-B	195
 β-D-gluco	Amberlite IRA 400 OH^-, MeOH, rt, 15 min	 (95) β-D-manno	II-B	195

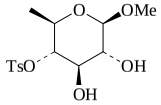
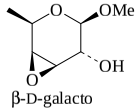
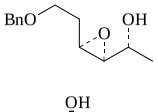
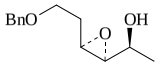
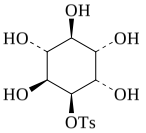
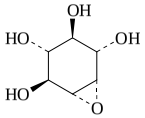
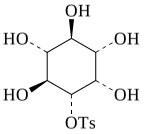
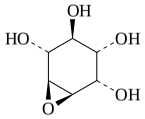
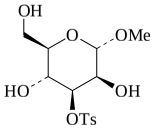
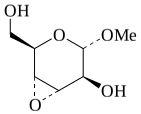
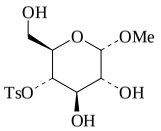
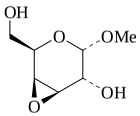
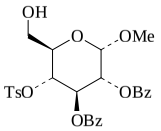
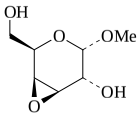
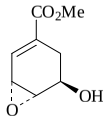
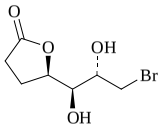
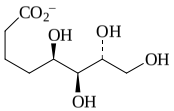
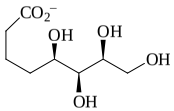
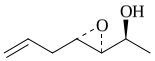
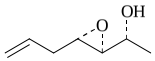
 β-D-gluco	Amberlite IRA 400 OH^-, MeOH, rt, 15 min	 β-D-galacto	(98)	II-B	195
	1. DEAD, Ph_3P, 4-$O_2NC_6H_4CO_2H$ 2. NaOMe, MeOH, rt, 25 min		(65)	I-B, IV	165
 1L-chiro	NaOMe, MeOH, rt, 4 h Deacidite FF (OH form) resin, MeOH, H_2O, 75–80°, 1h	 1L-myo	(60) (33)	II-B II-B	279 226
 1L-myo	NaOMe, DMSO, MeOH, rt, 2 h	 1L-chiro	(56)	II-B	279
 α-D-manno	NaOH, H_2O, 80°, dropwise	 α-D-altro	(79)	II-B	74

TABLE 7. CONDITIONS NOT LEADING TO EPOXIDE MIGRATION (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Related Table[b]	Refs.
 α-D-gluco	NaOMe, MeOH, $CHCl_3$, 0°, 5 h	 (74) α-D-galacto	II-B	53
 α-D-gluco	NaOMe, MeOH, $CHCl_3$, 0°, 5 h	 (81) α-D-galacto	II-B	53
C_7 	NaH or K_2CO_3, THF or MeOH	—[d]	II-A	219
	K_2CO_3, H_2O, rt, 24 h	 (72) +  (28)	I-B	32
	1. DEAD, Ph_3P, 4-$O_2NC_6H_4CO_2H$ 2. NaOMe, MeOH, rt, 25 min	 (76)	I-B, IV	165

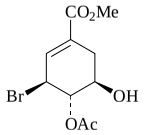
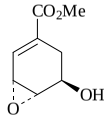
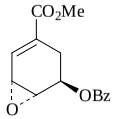
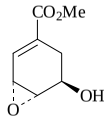
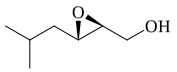
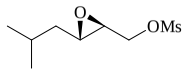
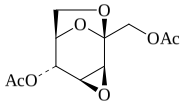
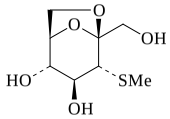
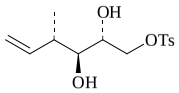
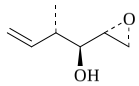
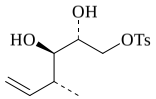
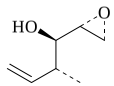
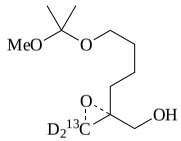
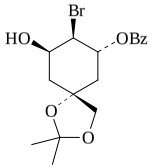
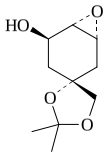
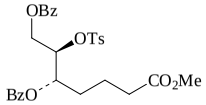
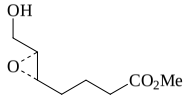
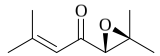
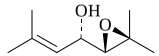
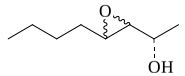
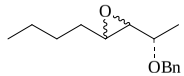
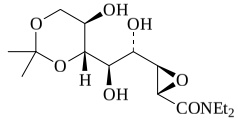
	NaOMe, MeOH, 0°, 30 min		(87)	II-B	143, 144
	MeO^-, 0°		(70)	II-B	280
	MsCl, py, 0°, 18 h		(91)	I-A, IV	281
 β-D-manno	NaSMe, MeOH, reflux, 2 h	 β-D-gluco	(65)	III-E	282
	NaOMe, MeOH, 4°, 10 min		(43)	I-B	200
	NaOMe, MeOH, 4°, 10 min		(50)	I-B	200

TABLE 7. CONDITIONS NOT LEADING TO EPOXIDE MIGRATION (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Related Table[b]	Refs.
	NaH, THF, reflux, 2 h	—[d]	I-A	24
	NaOMe, MeOH, THF, 0°	 (87)	II-B	234
	K_2CO_3, MeOH, 23°, 2 h	 (98)	I-B	283, 284
C_8 	$NaBH_4$, H_2O, Et_2O, rt, 30–45 min	 (55)	I-B	285
	NaH, BnBr, THF, rt, 1.5 h	 (73)	I-A	286
	KOH (0.1%), MeOH, rt, 66 days	—[d]	III-D	248

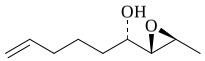
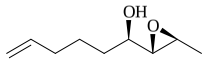
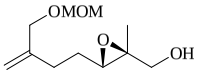
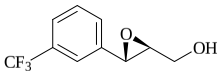
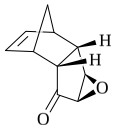
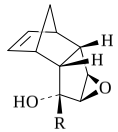
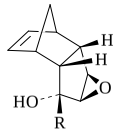
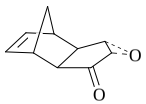
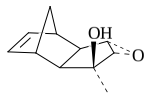
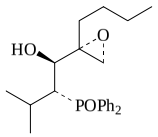
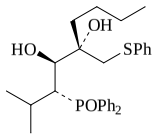
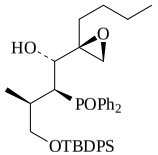
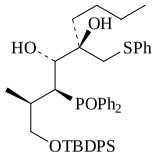
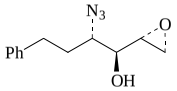
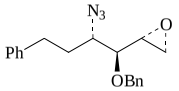
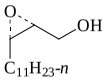
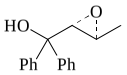
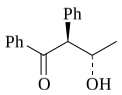
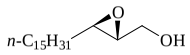
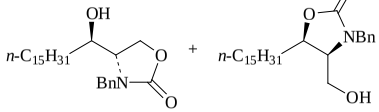
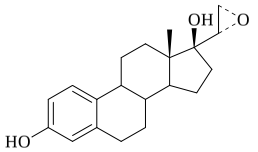
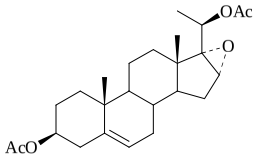
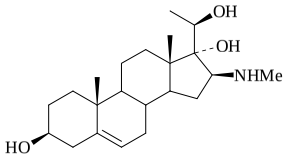
C_9		1. DEAD, Ph_3P, 4-$NO_2C_6H_4CO_2H$, rt, 12 h 2. NaOMe, MeOH, rt, 45 min	 (55)	I-A	198
		Unspecified cuprate reagents	—[d]	III-B	287
C_{10}		Base	—[d]	I-A	288
		$LiAlH_4$ or PhLi, THF, rt	 (50) R=H, Ph	II-B	84
				II-B	104
		RLi, THF, –20°, rapid addition RLi, THF, –20°, rapid addition RZnBr, THF	R (%) n-C_8H_{17} 83 $CH_2(CH_2)_7OTBDMS$ 95 $CH_2C{\equiv}CC_5H_{11}$-n 82		
		MeLi, THF, rt, 1 h	 (—)	II-B	84

TABLE 7. CONDITIONS NOT LEADING TO EPOXIDE MIGRATION (*Continued*)

	Substrate	Conditions	Product(s) and Yield(s) (%)	Related Table[b]	Refs.
C_{11}		PhSLi, THF	 (83)	I-A	208
		PhSLi, THF	 (83)	I-A	208
C_{12}		BnBr, *t*-Bu_4NI, NaH, THF, 25°, 1 h	 (80)	IV	289
C_{14}		Unspecified bases	—[d]	I-A	290
C_{16}		*t*-BuOK, *t*-BuOH, reflux, 4 h	 (72)	I-A	179

C_{18}		1. BnNCO, Et_3N, CH_2Cl_2, rt 2. NaH, THF, rt, 5 h	 **I** + **II** **I**:**II** = 58:42 (85)	IV	169
C_{20}		K_2CO_3, MeOH, rt	—[d] (—)	I-A	181
C_{21}		$MeNH_2$, TsOH (cat.), 130°, 4 d	 (58)	III-C	181

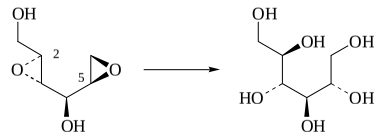
[a] Entries include only those reports for which the lack of epoxide migration was specifically noted.

[b] Other conditions leading to epoxide migration can be found in this table under the same carbon count.

[c] Compare 2,3-epoxycyclohexanone, Table II-B.

[d] No reaction was evident.

[e] For this product, the authors propose the opening of epoxide **I**, below, at C-2 and C-5, without epoxide migration.



I

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